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Prevalence of hyperuricemia in the eastern Chinese population

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3 **Prevalence of hyperuricemia in the eastern Chinese population**
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4 9 **Statement of authorship**

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6 10 The work has not been published previously, and not under consideration for publication
7
8 11 elsewhere. All authors have reviewed and approved the final version.

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10 12 **The author contribution lists**

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12 13 YL, BH designed and supervised this investigation. BH performed this investigation. YC,
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14 14 CFZ and YCC contributed to the data collection. NJW and QL provided technical or material
15
16 15 support. All authors read and approved the final manuscript.

17
18 16 **Data Sharing Statement**

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20 17 Please contact to corresponding author.

21
22 18 **Conflict of interests**

23
24 19 The authors have declared that no competing interests exist.

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54 34 **Ethical approval**

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56 35 The study protocol was approved by the Institutional Review Board of the Shanghai Ninth
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58 36 People's Hospital affiliated with Shanghai Jiaotong University School of Medicine.

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60 37 **Informed consent**

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60 38 Written consent was obtained from all the participants.

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39 **Patient and public involvement:**

40 Patients and the public were not involved in this study.

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4 41 **ABSTRACT**

5 42 **Objectives:** In the past decade, China has experienced a large scale of urbanization as well as
6
7 43 rapid economic growth. The aim of this study was to further investigate the prevalence of
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9 44 hyperuricemia (HUA) in the eastern Chinese population.

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11 45 **Design:** Cross-sectional study.

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13 46 **Setting:** SPECT-China study.

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15 47 **Participants:** In this study, 12,770 residents from 22 sites in eastern China were recruited.
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17 48 Finally, 9,225 subjects were included.

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19 49 **Main outcome measures:** The serum levels of uric acid, fasting blood glucose (FBG),
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21 50 HbA1c and other metabolic parameters were tested. The waist circumference (WC), weight,
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23 51 height and blood pressure were also measured. Questionnaires regarding smoking, drinking,
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25 52 education, etc. were collected from the subjects.

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27 53 **Results:** The prevalence of HUA in the eastern Chinese population was 12.3% (95%CI
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29 54 11.6-12.9%) overall, 17.9% (95%CI 16.7-19.1%) in men and 8.5% (95%CI 7.8-9.3%) in
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31 55 women. The incidence of HUA in urban subjects was higher than that in rural subjects (12.9
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33 56 vs. 10.8, $P<0.01$). The prevalence of HUA was decreased in men and increased in women.
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35 57 Residents with high BMI levels had a higher prevalence of HUA. In the logistic regression
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37 58 analysis, male sex, urban residency, TC, TG, overweight, obesity, SBP and low economic
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39 59 status were independently correlated with HUA.

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41 60 **Conclusions:** The estimated prevalence of HUA in the eastern Chinese population was 12.3%
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43 61 overall and 17.9% and 8.5% in men and women, respectively. HUA has gradually become an
44
45 62 important public health issue in China.

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47 63 **Trial registration:** ChiCTR-ECS-14005052

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49 64 **Key Words:** Prevalence, hyperuricemia, economic growth, public health, risk factors
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4 65 **Article summary**

5 66 **Strengths and limitations of this study**

67 The estimated prevalence of HUA in the eastern Chinese population was 12.3% overall and

68 17.9% and 8.5% in men and women, respectively.

69 This was a regional survey instead of a national study.

70 We did not consider the influence of diet.

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71 **Abbreviations:** HUA, hyperuricemia; FBG; fasting blood glucose; WC; waist circumference;
72 BMI, body mass index; LDL, low-density lipoprotein; TG, triglyceride; HDL, high-density
73 lipoprotein; TC, total cholesterol.

74 **Introduction**

75 In humans, uric acid is the end product of purine metabolism and is mainly excreted via the
76 kidneys. Xanthine oxidoreductase catalyzes two steps of enzymatic reactions, hypoxanthine
77 to xanthine and xanthine to uric acid. Several conditions could influence the concentration of
78 serum uric acid, including purine-rich food intake, neoplastic disease, cytotoxic drugs, obesity,
79 hypertension, etc [1-3].

80 Uric acid is reported to be associated with oxidative stress and inflammation [1, 4]. In
81 patients with hyperuricemia (HUA), deposition of uric acid in joints and tissues promotes the
82 occurrence of gout and chronic nephropathy. HUA has also been reported to be associated
83 with insulin resistance, NAFLD [5, 6] metabolic syndrome, type 2 diabetes, atherosclerosis
84 and coronary heart disease [7-11]. The overall prevalence of HUA in adults in the United
85 States was 21.4% in 2007-2008 [12]. However, in Chinese adults, the adjusted prevalence of
86 HUA in 2009-2010 was 8.4% [13].

87 In the past decade, China has experienced a large scale of urbanization. The percentage of
88 the urban population rose from 18% in 1978 to 56% in 2015 [14]. As serum uric acid is
89 closely related to economic development and urbanization [13], it was necessary to
90 understand the latest prevalence of HUA in China.

91 China is characterized by regional and economic diversity. Eastern China has a relatively
92 higher economic status than the rest of the country. In the present study, we performed a
93 cross-sectional survey to investigate the prevalence of HUA and its risk factors in the eastern
94 Chinese population.

95 **Methods**

96 **Study population**

97 Data of the current study are from SPECT-China, which is a population-based cross-sectional
98 survey on the prevalence of metabolic diseases and risk factors in Eastern China [15]. The
99 registration number is ChiCTR-ECS-14005052 (www.chictr.org). In this study, 12,770
100 residents from 22 sites in Shanghai, Zhejiang, Jiangsu, Anhui and Jiangxi provinces were
101 enrolled from January 2014 to December 2015. The inclusion and exclusion criteria were
102 described previously. We also excluded residents who had no uric acid data (n=3,535) and
103 CKD5 stage (n=10). Finally, 9,225 subjects were included (Figure 1). This study was
104 approved by the ethics committee of the Shanghai Ninth People's Hospital affiliated with
105 Shanghai Jiaotong University School of Medicine. Written consent was obtained from all the
106 participants.

108 **Measurements and definition**

109 HUA was defined as serum uric acid $> 420 \mu\text{mol/L}$ for men and $> 360 \mu\text{mol/L}$ for women
110 [16]. Blood pressure and heart rate was measured by a sphygmomanometer
111 (TERUMO-Elemano) three times. The mean of the three records was used in the analysis.
112 Hypertension was defined as a systolic blood pressure $\geq 140 \text{ mmHg}$ or diastolic blood
113 pressure $\geq 90 \text{ mmHg}$ or any self-reported history of hypertension. Diabetes was defined as a
114 self-reported history of diabetes or HbA1c levels of 6.5% or more. Prediabetes was defined as
115 HbA1c concentrations between 5.7% and 6.4%. Normal glucose tolerance (NGT) was defined
116 as an HbA1c less than 5.7% [17]. Weight and height were measured wearing light clothing
117 and without shoes. Body mass index (BMI) was calculated as weight (kg)/height squared (m^2).
118 Overweight was defined as $25 \text{ kg/m}^2 \leq \text{BMI} < 30 \text{ kg/m}^2$. Obesity was defined as $\text{BMI} \geq 30 \text{ kg/m}^2$.
119 Waist circumference (WC) was measured at the level of 1 cm above the umbilicus.
120 Demographic information and lifestyle risk factors were gathered from standard
121 questionnaires by trained staff. Current smoking was defined as having smoked at least 100
122 cigarettes in one's lifetime and currently smoking cigarettes [18]. Current drinking was
123 defined as drinking more than once a month. Current economic status was assessed by the
124 gross domestic product (GDP) per capita of 2013 in each study site. The mean national GDP

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4 125 per capita (6807 US dollars from World Bank) in 2013 was considered the cutoff point for
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6 126 economic status.

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10 128 **Assessment of biomarkers**

11 129 Venous blood samples were drawn from all participants after fasting for at least 8 hours and
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13 130 immediately centrifuged (2000 rpm for 15 min) at room temperature. Blood samples were
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15 131 stored at -20°C when collected and shipped by air in dry ice to one central laboratory certified
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17 132 by the College of American Pathologists within 2-4 hours of collection. All plasma and serum
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19 133 samples were frozen at -80°C after laboratory testing. Serum UA and other biochemical
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21 134 indexes were analyzed by a Beckman Coulter AU 680 device with the original kit. Insulin
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23 135 was tested by an Abbott i2000 SR analyzer with the original kit. HbA1c was detected using
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25 136 high-performance liquid chromatography (HPLC) by MQ-2000PT (Medconn Technology,
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27 137 Shanghai, China) using commercial reagents (HuaChen Biological Reagent Co., Ltd.,
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29 138 Shanghai, China).

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33 140 **Statistical analysis**

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35 141 Statistical analysis was performed using IBM SPSS Statistics, Version 22 (IBM Corporation,
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37 142 Armonk, New York). Demographic and metabolic characteristics are expressed as the mean ±
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39 143 SD or as the means (95% CI) for continuous variables and percentages (95% CI) for
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41 144 categorical variables in the overall population and in subgroups of location, age, economic
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43 145 status, BMI and glucose status. Logistic analysis was used to investigate the association of
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45 146 demographic, lifestyle, and metabolic factors with the odds of HUA. All analyses were
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47 147 two-sided. $P < 0.05$ was considered significant.

148 **Results**

149 **Characteristics of the eastern Chinese population**

150 In our study, we analyzed the uric acid in 9,225 Chinese adults, including 3,682 males (age,
151 55.57 ± 13.23 y) and 5,543 females (age 54.30 ± 12.82 y). Levels of serum uric acid were
152 352.12 ± 79.30 nmol/L and 269.29 ± 64.68 nmol/L in males and females, respectively. There
153 were significant differences between blood glucose, blood lipids, uric acid, BMI, WC and
154 blood pressure. The incidence of diabetes and hypertension also showed a significant
155 difference (Table 1).

157 **Metabolic risk factors of the eastern Chinese population**

158 The incidence of diabetes and hypertension, WC, SBP and BMI increased with age. As BMI
159 and glucose levels rose, the incidence of hypertension, WC, SBP, BMI, TG, FPG, and HbA1c
160 increased. Moreover, people living in rural areas had a higher incidence of diabetes, WC, SBP,
161 LDL, HDL, TC and HbA1c. People with a high economic status had a higher incidence of
162 diabetes, WC, UA, BMI, LDL, FPG, HbA1c and Cr (Tables 2, 3).

164 **Estimated prevalence of HUA in the eastern Chinese population**

165 The prevalence of HUA was 12.3% (95%CI 11.6, 12.9%), with 17.9% (95%CI 16.7, 19.1%)
166 and 8.5% (95%CI 7.8, 9.3%) in males and females, respectively. The prevalence of HUA in
167 urban areas was higher than that in rural areas (12.9% vs. 10.8%). The ratio of HUA in
168 developed areas was slightly higher than that in underdeveloped areas (12.6% vs. 11.8%). As
169 the BMI increased, the prevalence of HUA increased in both men and women. In women, the
170 proportion of HUA increased in normal, prediabetic and diabetic populations. However, this
171 trend was not obvious in men (Table 4).

173 **Logistic regression analysis of HUA**

174 Male sex, urban residency, increased TC or TG, overweight, obesity, elevated SBP and low
175 economic status were all risk factors for HUA in the eastern Chinese population (Table 5).
176 However, increased age, higher educational status, increased LDL or HDL, current smoking
177 or drinking and elevated DBP were not associated with the risk of HUA.

178 Discussion

179 In the Eastern population of China, the prevalence of HUA was 12.3% (95%CI 11.6-12.9%),
180 which was similar to the pooled prevalence of the systematic review in China (13.3%) [19].
181 However, this prevalence was more than that in the national HUA survey, which reported that
182 the prevalence of HUA was 8.4% [13]. The previous survey in China was performed in
183 2009-2010. Our study occurred in 2014-2015. These two studies investigated different
184 populations. In addition, our prevalence was relatively lower than that in Qingdao, which is
185 close to the sea and where residents consume high amounts of seafood and beer [20].
186 Moreover, the incidence of HUA in our population was lower than those in the United States
187 and Japan [12, 21], which might be attributed to economic status.

188 The prevalence of HUA in young men (<40 years) was six times more than that in young
189 women. However, as the age increased, the prevalence of HUA gradually decreased in men
190 and increased in women, which was coincident with values previously reported [22]. In
191 residents more than 70 years in age, men and women had a similar prevalence of HUA. We
192 deduced that the diet of young men contains more purine than that of old men. The young
193 men also had active metabolisms. The prevalence of HUA was dramatically increased in
194 women older than 50 years, which might be caused by reduced estrogen levels.

195 In previous studies, the prevalences of HUA in urban areas were much greater than those in
196 rural areas [13, 22]. However, in our study, the prevalence of HUA in urban areas was mildly
197 elevated (12.9% vs. 10.8%). Eastern China was the relatively developed area in the whole
198 country. Therefore, the difference between urban and rural areas was not obvious as in other
199 places.

200 Risk factors for HUA were also evaluated in our study. We found that male sex, urban
201 residency, hypertriglyceridemia, hypercholesterolemia, overweight, obesity, high SBP and
202 low economic status were risk factors for HUA. In previous studies, hypertriglyceridemia was
203 thought to be the strongest risk factor for HUA [22, 23]. However, the OR for HUA was 1.7
204 times with 1 SD elevation of triglyceridemia. In addition, obesity was the strongest risk factor
205 (OR=3.035) in our study. China has the largest obese population in the world [24]. In this
206 case, the prevalence of HUA will increase with the rising trend of obesity. Therefore, we
207 should pay more attention to prevent its consequence.

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208 HUA is closely related to lifestyle and dietary habits. In accordance with a previous study,
209 smoking was not associated with HUA [13]. However, according to a previous study, alcohol
210 intake influences the serum UA, which is different from the results of our study. This
211 difference might have been caused by our definition of current drinking (current drinking was
212 defined as drinking in the past 1 month), which mixed non-habitual drinkers and habitual
213 drinkers together.

214 As the age increased, UA together with components of metabolic syndrome (FPG, SBP,
215 WC) also increased, which indicated there might be a close relationship between metabolic
216 syndrome and HUA. Other studies have also found that HUA is associated with metabolic
217 syndrome [25, 26]. An epidemiologic study showed that HUA is positively correlated to
218 fasting serum insulin [27]. Krishnan et al reported that people with HUA have 1.36 times the
219 risk of developing insulin resistance in a 15-year follow-up study [28]. Thus, research has
220 indicated that insulin resistance plays an important role in the relationship between metabolic
221 syndrome and HUA [29].

222 There were several limitations in our study. First, this was not a national study but a local
223 survey. Second, we did not consider the influence of diet. Blood was drawn after fasting for
224 eight hours. However, the diet ingested near to the blood drawing time was unknown. In
225 addition, this was a cross-sectional study. Therefore, we could not identify a causal
226 relationship between HUA and its risk factors.

227 In this study, we estimated the prevalence of HUA in the eastern Chinese population. To
228 prevent the prevalence of HUA, more attention should be paid to life status (such as economic
229 status and residency localization) and metabolic indexes (TC, TG, BMI, and SBP).

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300 **Figure legend**

301 **Fig. 1** Flowchart of this study.

302 We totally collected 12, 770 subjects. After excluding participants who had missing data.

303 Finally, 9, 225 subjects were included

304 **Table 1** Baseline characteristics between different groups.

Variables	Men (n=3682)	Women (n=5543)	P value
Age y	55.57±13.23	54.30±12.82	0.000
FPS mmol/L	5.72±1.63	5.50±1.36	0.000
HbA1c %	5.78±1.08	5.64±0.92	0.000
TG mmol/L	1.88±1.79	1.55±1.20	0.000
TC mmol/L	5.14±1.13	5.27±1.15	0.000
LDL mmol/L	3.23±0.77	3.30±0.83	0.000
HDL mmol/L	1.30±0.31	1.45±0.32	0.000
Uric acid umol/L	352.12±79.30	269.29±64.68	0.000
BMI kg/m ²	25.11±3.45	24.40±3.67	0.000
WC cm	85.85±9.42	78.72±9.90	0.000
SBP mmHg	134.31±20.71	131.12±22.22	0.000
DBP mmHg	82.12±12.90	77.77±12.93	0.000
Diabetes %	16.3%	12.7%	0.000
Hypertension %	53.4%	44.1%	0.000

305 Fasting plasma glucose: FPG; Alanine aminotransferase: ALT; Triglycerides: TG; Total
 306 cholesterol: TC; Body mass index: BMI; Waist circumference: WC; Systolic blood pressure: SBP;
 307 Diastolic blood pressure: DBP

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Table 2 Characteristics of Eastern Chinese population.

	% (95%CI)				Mean (95%CI)		
	Diabetes	Hypertension	Smoking	Drinking	WC	SBP	BMI
Overall	14.1 (13.4, 14.8)	47.8 (46.8, 48.9)	19.2 (18.3, 20.0)	55.8 (54.8, 56.9)	81.58 (81.37, 81.79)	132.38 (131.93, 132.83)	24.69 (24.62, 24.77)
Location							
Rural	15.8 (14.4, 17.2)	58.7 (56.8, 60.6)	22.9 (21.3, 24.5)	56.6 (54.7, 58.5)	83.14 (82.75, 83.54)	139.74 (138.86, 140.63)	24.71 (24.57, 24.85)
Urban	13.4 (12.6, 14.2)	43.3 (42.1, 44.5)	17.6 (16.7, 18.6)	55.5 (54.3, 56.7)	80.90 (80.65, 81.16)	129.35 (128.85, 129.84)	24.67 (24.59, 24.76)
Age groups							
<40	1.6 (0.9, 2.3)	11.1 (9.4, 12.9)	12.9 (11.0, 14.8)	42.0 (39.2, 44.7)	75.22 (74.63, 75.82)	116.83 (115.99, 117.67)	23.38 (23.18, 23.58)
40-50	5.9 (4.8, 7.0)	31.6 (29.4, 33.7)	17.1 (15.3, 18.9)	53.2 (50.9, 55.6)	78.95 (78.48, 79.42)	125.59 (124.71, 126.46)	24.56 (24.41, 24.72)
50-60	15.3 (13.8, 16.7)	49.4 (47.4, 51.4)	23.5 (21.8, 25.2)	56.2 (54.2, 58.2)	82.14 (81.76, 82.52)	132.39 (131.57, 133.21)	25.02 (24.88, 25.15)
60-70	20.3 (18.8, 21.9)	62.3 (60.4, 64.2)	19.5 (17.9, 21.0)	61.5 (59.6, 63.4)	84.00 (83.63, 84.36)	138.84 (138.00, 139.68)	25.06 (24.91, 25.21)
>70	24.4 (21.9, 26.9)	78.5 (76.0, 80.9)	19.1 (16.7, 21.5)	61.6 (58.7, 64.6)	86.02 (85.42, 86.62)	146.05 (144.81, 147.29)	24.73 (24.51, 24.95)
Economic status							
low	12.3 (11.3, 13.3)	47.8 (46.3, 49.4)	21.2 (19.9, 22.5)	46.6 (45.1, 48.2)	81.07 (80.74, 81.39)	134.20 (133.47, 134.93)	24.50 (24.39, 24.61)
high	15.6 (14.6, 16.6)	47.8 (46.4, 49.2)	17.6 (16.5, 18.6)	62.9 (61.6, 64.3)	81.96 (81.68, 82.24)	130.97 (130.42, 131.52)	24.83 (24.73, 24.93)
BMI							
<25	10.5 (9.7, 11.3)	38.0 (36.7, 39.4)	17.3 (16.3, 18.4)	54.1 (52.7, 55.5)	76.16 (75.94, 76.39)	128.30 (127.72, 128.89)	22.28 (22.23, 22.33)
25-29.9	17.7 (16.4, 19.0)	57.9 (56.2, 59.6)	20.7 (19.3, 22.1)	57.9 (56.2, 59.6)	87.24 (86.99, 87.50)	136.79 (136.06, 137.51)	26.98 (26.94, 27.03)
>=30	26.2 (22.6, 29.7)	73.1 (69.6, 76.7)	24.6 (21.1, 28.1)	59.0 (55.0, 62.9)	96.39 (95.64, 97.15)	142.00 (140.43, 143.57)	32.51 (32.21, 32.81)
Glucose status							
normal	-	37.0 (35.6, 38.3)	16.2 (15.1, 17.2)	50.6 (49.3, 52.0)	78.95 (78.68, 79.22)	127.98 (127.42, 128.55)	24.08 (23.99, 24.18)

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prediabetes	-	57.6 (55.7, 59.5)	23.4 (21.7, 25.0)	63.2 (61.3, 65.1)	83.90 (83.52, 84.27)	136.70 (135.85, 137.54)	25.26 (25.12, 25.40)
diabetes	-	72.7 (70.3, 75.2)	23.0 (20.6, 25.3)	61.3 (58.7, 64.0)	87.60 (87.05, 88.15)	141.93 (140.76, 143.09)	26.00 (25.80, 26.21)

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Table 3 Biochemical index of Eastern Chinese population.

	Mean (95%CI)							
	UA	LDL	TG	HDL	TC	FPG	HbA1c	Cr
Overall	301.84 (300.14, 303.53)	3.28 (3.26, 3.29)	1.68 (1.65, 1.71)	1.39 (1.38, 1.39)	5.22 (5.19, 5.24)	5.59 (5.56, 5.62)	5.70 (5.67, 5.72)	77.35 (77.04, 77.65)
Location								
Rural	294.82 (291.72, 297.92)	3.38 (3.35, 3.41)	1.69 (1.63, 1.75)	1.44 (1.43, 1.45)	5.37 (5.33, 5.41)	5.63 (5.57, 5.69)	5.80 (5.76, 5.84)	73.76 (73.22, 74.29)
Urban	305.55 (303.58, 307.53)	3.23 (3.21, 3.25)	1.67 (1.64, 1.71)	1.37 (1.36, 1.37)	5.16 (5.13, 5.18)	5.57 (5.53, 5.60)	5.65 (5.63, 5.67)	78.87 (78.51, 79.24)
Age groups								
<40	294.08 (289.32, 298.85)	2.80 (2.77, 2.84)	1.35 (1.28, 1.42)	1.39 (1.37, 1.40)	4.60 (4.55, 4.65)	4.98 (4.94, 5.02)	5.09 (5.06, 5.12)	75.82 (75.00, 76.63)
40-50	287.23 (283.32, 291.14)	3.10 (3.07, 3.13)	1.68 (1.59, 1.77)	1.40 (1.39, 1.42)	5.02 (4.97, 5.07)	5.33 (5.27, 5.38)	5.40 (5.36, 5.44)	75.05 (74.39, 75.71)
50-60	305.93 (302.74, 309.12)	3.43 (3.39, 3.46)	1.82 (1.76, 1.88)	1.39 (1.37, 1.40)	5.42 (5.37, 5.46)	5.67 (5.60, 5.73)	5.78 (5.74, 5.82)	77.17 (76.58, 77.75)
60-70	306.36 (303.39, 309.32)	3.44 (3.41, 3.47)	1.74 (1.69, 1.79)	1.38 (1.37, 1.39)	5.42 (5.37, 5.46)	5.80 (5.74, 5.86)	5.95 (5.91, 5.99)	77.64 (77.08, 78.20)
>70	318.74 (314.05, 323.43)	3.37 (3.32, 3.42)	1.58 (1.53, 1.63)	1.38 (1.36, 1.40)	5.34 (5.28, 5.40)	6.00 (5.90, 6.10)	6.06 (6.00, 6.12)	82.43 (81.45, 83.40)
Economic status								
low	299.75 (297.15, 302.35)	3.23 (3.20, 3.25)	1.70 (1.65, 1.75)	1.45 (1.44, 1.46)	5.20 (5.17, 5.24)	5.54 (5.49, 5.58)	5.62 (5.59, 5.65)	76.29 (75.82, 76.75)
high	304.44 (302.28, 306.60)	3.31 (3.29, 3.34)	1.66 (1.63, 1.70)	1.34 (1.33, 1.35)	5.23 (5.20, 5.26)	5.62 (5.58, 5.66)	5.75 (5.72, 5.78)	78.20 (77.79, 78.60)
BMI								
<25	284.75 (282.68, 286.82)	3.19 (3.17, 3.21)	1.44 (1.41, 1.47)	1.45 (1.44, 1.46)	5.13 (5.10, 5.16)	5.42 (5.38, 5.45)	5.56 (5.53, 5.58)	76.19 (75.79, 76.58)
25-29.9	321.87 (319.05, 324.69)	3.39 (3.36, 3.42)	1.94 (1.89, 1.99)	1.30 (1.29, 1.31)	5.32 (5.28, 5.36)	5.74 (5.69, 5.79)	5.84 (5.80, 5.87)	78.88 (78.35, 79.42)
≥30	339.36 (332.47, 346.25)	3.44 (3.37, 3.50)	2.33 (2.11, 2.54)	1.27 (1.25, 1.29)	5.40 (5.32, 5.49)	6.12 (5.96, 6.27)	6.12 (6.02, 6.21)	78.32 (77.11, 79.53)
Glucose status								
normal	294.93 (292.74, 297.12)	3.12 (3.10, 3.14)	1.54 (1.51, 1.58)	1.41 (1.40, 1.42)	5.05 (5.02, 5.08)	5.09 (5.07, 5.10)	5.16 (5.15, 5.17)	76.81 (76.41, 77.21)

prediabetes	313.08 (309.95, 316.22)	3.51 (3.48, 3.54)	1.71 (1.66, 1.75)	1.38 (1.37, 1.40)	5.49 (5.44, 5.53)	5.45 (5.42, 5.48)	5.93 (5.92, 5.94)	77.95 (77.38, 78.52)
diabetes	310.93 (306.50, 315.36)	3.42 (3.38, 3.47)	2.18 (2.06, 2.30)	1.29 (1.27, 1.31)	5.38 (5.31, 5.45)	7.89 (7.75, 8.04)	7.38 (7.30, 7.46)	78.22 (77.33, 79.12)

Table 4 Estimated prevalence of HUA in Eastern Chinese population.

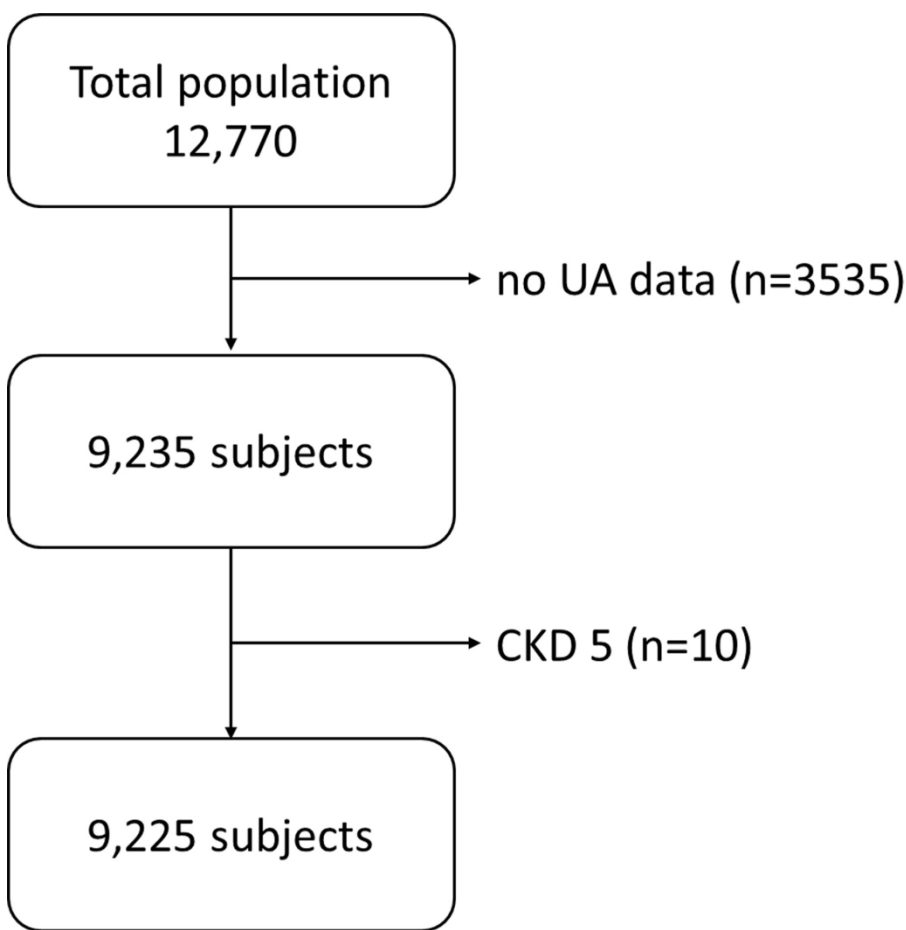
	% (95%CI)		
	Overall	Men	Women
Overall	12.3 (11.6, 12.9)	17.9 (16.7-19.1)	8.5 (7.8-9.3)
Location			
Urban	12.9 (12.1, 13.7)	19.1 (17.6-20.7)	8.9 (8.0-9.8)
Rural	10.8 (9.6, 12.0)	15.2 (13.1-17.3)	7.7 (6.4-9.0)
Age groups			
<40	10.8 (9.0-12.5)	22.8 (19.0-26.6)	3.3 (2.0-4.5)
40-50	9.0 (7.6-10.3)	19.3 (16.3-22.3)	3.1 (2.1-4.1)
50-60	12.9 (11.6-14.3)	18.6 (16.1-21.0)	9.2 (7.7-10.6)
60-70	13.1 (11.8-14.4)	15.3 (13.1-17.5)	11.6 (10.0-13.2)
>70	15.9 (13.8-18.0)	15.6 (12.5-18.7)	16.1 (13.2-19.1)
Economic status			
low	11.8 (10.9-12.8)	18.3 (16.5-20.1)	7.2 (6.1-8.2)
high	12.6 (11.7-13.5)	17.5 (15.8-19.2)	9.5 (8.5-10.6)
BMI			
<25	7.8 (7.0-8.5)	12.4 (10.9-13.9)	5.2 (4.5-6.0)
25-29.9	16.4 (15.1-17.7)	22.0 (19.9-24.1)	11.6 (10.1-13.1)
≥30	25.9 (22.4-29.4)	30.2 (24.6-35.8)	22.5 (18.1-27.0)
Glucose status			
normal	10.1 (9.3-10.9)	17.5 (15.8-19.2)	5.7 (4.9-6.5)
prediabetes	15.2 (13.9-16.6)	20.3 (17.9-22.7)	11.6 (10.0-13.2)
diabetes	15.1 (13.1-17.0)	15.0 (12.1-17.8)	15.2 (12.5-17.9)

Table 5 Risk factors for HUA in Eastern Chinese population.

Risk factors	OR	(95%CI)
Female sex	0.502	0.420, 0.599
Age per 10 years	1.039	0.974, 1.109
Urban residency	2.208	1.674, 2.913
≥Junior middle school education	1.050	0.873, 1.263
Lipids		
LDL per 1SD	1.033	0.900, 1.185
HDL per 1SD	0.925	0.840, 1.019
TC per 1SD	1.218	1.043, 1.422
TG per 1SD	1.701	1.517, 1.906
Current smoking	0.941	0.777, 1.139
Current drinking	0.916	0.787, 1.066
BMI		
Overweight	1.770	1.509, 2.075
Obesity	3.035	2.385, 3.862
Blood pressure		
SBP per 10mmHg	1.059	1.013, 1.108
DBP per 10mmHg	1.011	0.943, 1.084
High economic status	0.693	0.543, 0.886

Data are expressed as unStandardized B (95%CI). The enter procedure was used.

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STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	7
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	7,8
Data sources/measurement	8*	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Bias	9	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Study size	10	Describe any efforts to address potential sources of bias	7
Quantitative variables	11	Explain how the study size was arrived at	8
Statistical methods	12	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
		(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	8
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	8
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	8
		(e) Describe any sensitivity analyses	8

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	7
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(b) Report category boundaries when continuous variables were categorized	9
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Prevalence of hyperuricemia in an eastern Chinese population: a cross-sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-035614.R1
Article Type:	Original research
Date Submitted by the Author:	11-Feb-2020
Complete List of Authors:	Han, Bing; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Wang, Ningjian; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Chen, Yi; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Li, Qin; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Zhu, Chunfang ; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Chen, Yingchao; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Lu, Yingli; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology
Keywords:	General endocrinology < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY, Diabetes & endocrinology < INTERNAL MEDICINE

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3 **1 Prevalence of hyperuricemia in an eastern Chinese population: a cross-sectional**
4 **2 study**

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20 9 Running title: Prevalence of hyperuricemia in China.
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60**10 Statement of authorship**

11 The work has not been published previously, and not under consideration for publication
12 elsewhere. All authors have reviewed and approved the final version.

13 The author contribution lists

14 YL, BH designed and supervised this investigation. BH performed this investigation. YC,
15 CFZ and YCC contributed to the data collection. NJW and QL provided technical or material
16 support. All authors read and approved the final manuscript.

17 Data Sharing Statement

18 Please contact to corresponding author.

19 Conflict of interests

20 The authors have declared that no competing interests exist.

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23 Compliance with Ethical Standards

24 All procedures performed in this study were in accordance with the principles of the Helsinki
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35 analysis, or interpretation of data or in the preparation, review, or approval of the article.

36 Ethical approval

37 The study protocol was approved by the Institutional Review Board of the Shanghai Ninth
38 People's Hospital affiliated with Shanghai Jiaotong University School of Medicine.

39 Informed consent

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4 40 Written consent was obtained from all the participants.
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6 41 **Patient and public involvement:**
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8 42 Patients and the public were not involved in this study.
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4 43 **ABSTRACT**

5 44 **Objectives:** In the past decade, China has been characterized by large-scale urbanization as
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7 45 well as rapid economic growth. The aim of this study was to further investigate the
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9 46 prevalence of hyperuricemia (HUA) in an eastern Chinese population.

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11 47 **Design:** Cross-sectional study.

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13 48 **Setting:** Survey of Prevalence in East China of Metabolic Diseases and Risk Factors
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15 49 (SPECT-China) study.

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17 50 **Participants:** In this study, 12,770 residents from 22 sites in eastern China were recruited.
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19 51 Finally, 9,225 subjects were included.

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21 52 **Main outcome measures:** The serum levels of uric acid, fasting plasma glucose (FPG),
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23 53 glycated hemoglobin (HbA1c) and other metabolic parameters were tested. Waist
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25 54 circumference (WC), weight, height and blood pressure were also measured. Questionnaires
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27 55 regarding smoking, drinking, education, etc., were collected from the subjects.

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29 56 **Results:** The prevalence of HUA in this eastern Chinese population was 11.3% (9.9, 12.7)
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31 57 overall, 20.7% (17.7, 23.7) in men and 5.6% (4.3, 6.7) in women. The prevalence of HUA in
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33 58 urban subjects was higher than that in rural subjects (12.9 vs. 10.8%, $P<0.01$). The prevalence
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35 59 of HUA was negatively and positively associated with age in men and women, respectively.
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37 60 Residents with high body mass index (BMI) levels had a higher prevalence of HUA. In the
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39 61 logistic regression analysis, male sex, urban residency, total cholesterol (TC), triglyceride
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41 62 (TG), overweight, obesity, systolic blood pressure (SBP) and low economic status were
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43 63 independently correlated with HUA.

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45 64 **Conclusions:** The estimated prevalence of HUA in this eastern Chinese population was
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47 65 11.3% (9.9, 12.7) overall and 20.7% (17.7, 23.7) and 5.6% (4.3, 6.7) in men and women,
48
49 66 respectively. HUA has gradually become an important public health issue in China.

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51 67 **Trial registration:** ChiCTR-ECS-14005052.

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53 68 **Keywords:** Prevalence, hyperuricemia, economic growth, public health, risk factors
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4 **69 Strengths and limitations of this study**

5 70 This is the largest published hyperuricemia study in an eastern Chinese population.

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7 71 This study covers residents from 22 sites in five provinces.

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9 72 This is a regional survey instead of a national study.

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11 73 This is a cross-sectional study that indicated an association between uric acid and other risk
12 factors.
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15 75 We do not consider the influence of diet.
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4 76 **Abbreviations:** HUA, hyperuricemia; FPG, fasting plasma glucose; WC; waist
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6 77 circumference; BMI, body mass index; LDL, low-density lipoprotein; TG, triglyceride; HDL,
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8 78 high-density lipoprotein; TC, total cholesterol; HbA1c, Glycated hemoglobin; SBP, systolic
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10 79 blood pressure; DBP, diastolic blood pressure; NAFLD, Nonalcoholic fatty liver disease;
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12 80 CKD, chronic kidney disease; NGT, Normal glucose tolerance; GDP, gross domestic product;
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14 81 HPLC, high-performance liquid chromatography
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82 Introduction

83 In humans, uric acid (UA) is the end product of purine metabolism and is mainly excreted via
84 the kidneys. Xanthine oxidoreductase catalyzes two enzymatic reactions, hypoxanthine to
85 xanthine and xanthine to UA. Several conditions can influence the concentration of serum UA,
86 including purine-rich food intake, neoplastic disease, cytotoxic drugs, obesity, hypertension,
87 etc. [1-3].

88 Uric acid is reported to be associated with oxidative stress and inflammation [1, 4]. In
89 patients with hyperuricemia (HUA), deposition of UA in joints and tissues promotes the
90 occurrence of gout and chronic nephropathy. HUA has also been reported to be associated
91 with insulin resistance, nonalcoholic fatty liver disease (NAFLD) [5, 6], metabolic syndrome,
92 type 2 diabetes, atherosclerosis and coronary heart disease [7-11]. The overall prevalence of
93 HUA in adults in the United States was 21.4% in 2007-2008 [12]. However, in Chinese adults,
94 the adjusted prevalence of HUA in 2009-2010 was 8.4% [13]. In an elderly Chinese
95 population, the overall prevalence of HUA was 13.1% [14]. Liu R et al [15] conducted a
96 meta-analysis between 2000 and 2014 to determine the prevalence of HUA in mainland China.
97 The pooled prevalence of HUA was 13.3% (male 19.4% and female 7.9%).

98 In the past decade, China has been characterized by large-scale urbanization. The
99 percentage of the urban population rose from 18% in 1978 to 56% in 2015 [16]. As serum UA
100 is closely related to economic development and urbanization [13], it is necessary to
101 understand the latest prevalence of HUA in China.

102 China is characterized by regional and economic diversity. Eastern China has a relatively
103 higher economic status than the rest of the country. In the present study, we performed a
104 cross-sectional survey to investigate the prevalence of HUA and its risk factors in an eastern
105 Chinese population.

106 **Methods**

107 **Study population**

108 Data from the current study are from the Survey of Prevalence in East China of Metabolic
109 Diseases and Risk Factors (SPECT-China), which is a population-based cross-sectional
110 survey of the prevalence of metabolic diseases and risk factors in eastern China [17]. The
111 registration number is ChiCTR-ECS-14005052 (www.chictr.org). In this study, 12,770
112 residents from 22 sites in Shanghai, Zhejiang, Jiangsu, Anhui and Jiangxi provinces were
113 enrolled from January 2014 to December 2015 (Supplemental Figure 1). The inclusion and
114 exclusion criteria were described previously [17]. Chinese citizens more than 18 years old
115 who had lived in their current area for more than 6 months were selected. We excluded
116 subjects with severe communication problems, acute illness, or an unwillingness to participate.
117 We also excluded residents who had no UA data (n=3,535) and chronic kidney disease (CKD)
118 stage 5 (n=10). Finally, 9,225 subjects were included. This study was approved by the ethics
119 committee of the Shanghai Ninth People's Hospital affiliated with Shanghai Jiaotong
120 University School of Medicine. Written consent was obtained from all the participants.

122 **Measurements and definition**

123 HUA was defined as serum UA >420 $\mu\text{mol/L}$ for men and >360 $\mu\text{mol/L}$ for women [18].
124 Blood pressure and heart rate were measured with a sphygmomanometer
125 (TERUMO-Elemano) three times. The mean of the three records was used in the analysis.
126 Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood
127 pressure (DBP) ≥ 90 mmHg or any self-reported history of hypertension. Diabetes was
128 defined as a self-reported history of diabetes or glycated hemoglobin (HbA1c) levels of 6.5%
129 or more. Prediabetes was defined as HbA1c concentrations between 5.7% and 6.4%. Normal
130 glucose tolerance (NGT) was defined as an HbA1c less than 5.7% [19]. Weight and height
131 were measured wearing light clothing and without shoes. Body mass index (BMI) was
132 calculated as weight (kg)/height squared (m^2). Overweight was defined as $24 \text{ kg/m}^2 \leq \text{BMI} < 28$
133 kg/m^2 . Obesity was defined as $\text{BMI} \geq 28 \text{ kg/m}^2$. Waist circumference (WC) was measured at
134 the level of 1 cm above the umbilicus. Demographic information and lifestyle risk factors
135 were gathered from standard questionnaires by trained staff. Current smoking was defined as

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4 136 having smoked at least 100 cigarettes in one's lifetime and currently smoking cigarettes [20].
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6 137 Current drinking was defined as drinking more than once a month. Current economic status
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8 138 was assessed by the gross domestic product (GDP) per capita of 2013 at each study site. The
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10 139 mean national GDP per capita (6807 US dollars from World Bank) in 2013 was considered
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12 140 the cutoff point for economic status.

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15 142 **Assessment of biochemical indexes**

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17 143 Venous blood samples were drawn from all participants after fasting for at least 8 hours and
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19 144 immediately centrifuged (2000 rpm for 15 min) at room temperature. Blood samples were
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21 145 stored at -20°C when collected and shipped by air in dry ice to one central laboratory certified
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23 146 by the College of American Pathologists within 2-4 hours of collection. All plasma and serum
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25 147 samples were frozen at -80°C after laboratory testing. Serum UA was analyzed with a
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27 148 Beckman Coulter AU 680 device with the original kit (Brea, California, USA). The validity
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29 149 and accuracy of UA were 6% and 4%, respectively. Other biochemical indexes were analyzed
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31 150 as described previously [21].

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34 152 **Statistical analysis**

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36 153 Statistical analysis was performed using IBM SPSS Statistics, Version 22 (IBM Corporation,
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38 154 Armonk, New York). Demographic and metabolic characteristics are expressed as the mean ±
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40 155 SD for continuous variables and percentages (95% CI) for categorical variables in the overall
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42 156 population and in subgroups of location, age, economic status, BMI and glucose status.
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44 157 Logistic analysis was used to investigate the association of demographic, lifestyle, and
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46 158 metabolic factors with the odds of HUA. According to the 6th national population census data,
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48 159 the proportions of the population in different age groups (<40, 40-60, ≥60) are 57.39%,
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50 160 29.29%, and 13.31% (total); 58.10%, 29.13%, and 12.76% (male); and 56.61%, 29.46%, and
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52 161 13.91% (female), respectively (<http://www.stats.gov.cn/tjsj/pcsj/rkpc/6rp/indexce.htm>). Thus,
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54 162 we adjusted the prevalence of HUA by these proportions. All analyses were two-sided.
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56 163 $P < 0.05$ was considered significant.

164 **Results**

165 **Characteristics of this eastern Chinese population**

166 In our study, we analyzed UA in 9,225 Chinese adults, including 3,682 males (age,
167 55.57±13.23 y) and 5,543 females (age 54.30±12.82 y). The mean levels of serum UA were
168 352.12±79.30 nmol/L and 269.29±64.68 nmol/L in males and females, respectively. There
169 were significant sex differences in blood glucose, blood lipids, UA, BMI, WC and blood
170 pressure. The prevalence of diabetes and hypertension also showed a significant difference
171 (Table 1).

173 **Metabolic risk factors of this eastern Chinese population**

174 The prevalence of diabetes and hypertension, WC, SBP and BMI increased with age. As BMI
175 and glucose levels rose, the prevalence of hypertension, WC, SBP, BMI, triglyceride (TG),
176 FPG, and HbA1c increased. Moreover, people living in rural areas had a higher prevalence of
177 diabetes, WC, SBP, low-density lipoprotein (LDL), high-density lipoprotein (HDL), total
178 cholesterol (TC) and HbA1c. People with a high economic status had a higher prevalence of
179 diabetes, WC, UA, BMI, LDL, FPG, HbA1c and Cr (Tables 2, 3).

181 **Estimated prevalence of HUA in this eastern Chinese population**

182 The prevalence of HUA was 12.3% (11.6, 12.9), with 17.9% (16.7, 19.1) and 8.5% (7.8, 9.3)
183 in males and females, respectively. The prevalence of HUA in urban areas was higher than
184 that in rural areas (12.9% vs. 10.8%). The prevalence of HUA in developed areas was slightly
185 higher than that in underdeveloped areas (12.6% vs. 11.8%). As BMI increased, the
186 prevalence of HUA increased in both men and women. In women, the prevalence of HUA
187 increased in normal, prediabetic and diabetic populations. However, this trend was not
188 obvious in men. After adjusting for the proportions of the population in different age groups,
189 the prevalence of HUA was 11.3% (9.9, 12.7), with 20.7% (17.7, 23.7) and 5.6% (4.3, 6.7) in
190 males and females, respectively (Table 4). When HUA was defined as serum UA of more
191 than 420 µmol/L in both men and women, the prevalence of HUA was 8.4% (7.8, 9.0), with
192 17.9% (16.7, 19.1) and 2.1% (1.7, 2.5) in males and females, respectively. After adjusting for
193 the proportions of the population in different age groups, the prevalence of HUA was 8.8%

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4 194 (7.5, 10.1), with 20.7% (17.7, 23.7) and 1.4% (0.7, 2.0) in males and females, respectively
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6 195 (Supplemental Table 1).

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10 197 **Logistic regression analysis of HUA**

11 198 Male sex, urban residency, increased TC or TG, overweight, obesity, elevated SBP and low
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13 199 economic status were all risk factors for HUA in this eastern Chinese population (Table 5).

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15 200 However, increased age, higher educational status, increased LDL or HDL, current smoking
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17 201 or drinking and elevated DBP were not associated with the risk of HUA. When HUA was
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19 202 defined as serum UA of more than 420 $\mu\text{mol/L}$ in both men and women, the association was
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21 203 similar to the above results (Supplemental Table 2).

204 Discussion

205 In this eastern Chinese population, the prevalence of HUA was 11.3%, which was similar to
206 the pooled prevalence reported in a systematic review performed in China (13.3%) [15].
207 However, this prevalence was more than that in the national HUA survey, which reported that
208 the prevalence of HUA was 8.4% [13]. The previous survey was performed in 2009-2010.
209 Our study occurred in 2014-2015. These two studies investigated different populations. In
210 addition, our prevalence was relatively lower than that in Qingdao, which is close to the sea
211 and where residents consume high amounts of seafood and beer [22]. Moreover, the
212 prevalence of HUA in our population was lower than those in the United States and Japan [12,
213 23], which might be attributed to economic status.

214 The prevalence of HUA in young men (<40 years) was seven times greater than that in
215 young women. However, as age increased, the prevalence of HUA gradually decreased in
216 men and increased in women, which was coincident with values previously reported [24]. In
217 residents more than 60 years of age, men and women had a similar prevalence of HUA. We
218 deduced that the diet of young men contains more purine than that of old men. The young
219 men also had an active metabolism. The prevalence of HUA was dramatically increased in
220 women older than 60 years, which might be caused by reduced estrogen levels.

221 Risk factors for HUA were also evaluated in our study. We found that male sex, urban
222 residency, hypertriglyceridemia, hypercholesterolemia, overweight, obesity, high SBP and
223 low economic status were risk factors for HUA. In previous studies, hypertriglyceridemia was
224 thought to be the strongest risk factor for HUA [24, 25]. However, the OR for HUA was 1.7
225 times with 1 SD elevation of triglyceridemia. In addition, obesity was the strongest risk factor
226 (OR=2.874) in our study. China has the largest obese population in the world [26]. In this
227 case, the prevalence of HUA will increase with the rising trend of obesity. Therefore, we
228 should pay more attention to prevent its consequences.

229 HUA is closely related to lifestyle and dietary habits. In previous studies, the prevalence of
230 HUA in urban areas was much greater than that in rural areas [13, 24]. In our study, the
231 prevalence of HUA in urban areas was mildly elevated (12.9% vs. 10.8%), and urbanization
232 was a risk factor for HUA. Eastern China is considered the developed area in the whole
233 country. Therefore, the difference between urban and rural areas was not obvious as in other

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4 234 places. Moreover, people with high economic status consumed more healthy food that
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6 235 contained low purine ingredients. This could partly explain why low economic status became
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8 236 a risk factor for HUA. In accordance with a previous study, smoking was not associated with
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10 237 HUA [13]. However, according to a previous study, alcohol intake influences serum UA,
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12 238 which is different from the results of our study. This difference might have been caused by
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14 239 our definition of current drinking (current drinking was defined as drinking in the past 1
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16 240 month), which mixed nonhabitual drinkers and habitual drinkers together.

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18 241 As age increased, UA together with components of metabolic syndrome (FPG, SBP, WC)
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20 242 also increased, which indicated that there might be a close relationship between metabolic
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22 243 syndrome and HUA. Other studies have also found that HUA is associated with metabolic
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24 244 syndrome [27, 28]. An epidemiologic study showed that HUA is positively correlated with
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26 245 fasting serum insulin [29]. Krishnan et al reported that people with HUA have 1.36 times the
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28 246 risk of developing insulin resistance in a 15-year follow-up study [30]. Thus, research has
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30 247 indicated that insulin resistance plays an important role in the relationship between metabolic
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32 248 syndrome and HUA [31].

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34 249 There were several limitations in our study. First, this was not a national study but a local
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36 250 survey. Second, we did not consider the influence of diet. Blood was drawn after fasting for
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38 251 eight hours. However, the diet ingested near the blood drawing time was unknown. In
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40 252 addition, this was a cross-sectional study. Therefore, we could not identify a causal
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42 253 relationship between HUA and its risk factors.

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44 254 In this study, we estimated the prevalence of HUA in an eastern Chinese population. To
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46 255 prevent the prevalence of HUA, more attention should be paid to life status (such as economic
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48 256 status and residence) and metabolic indexes (TC, TG, BMI, and SBP).
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4 331 **Figure legend**

5 332 **Supplemental Figure 1** Position of the 5 provinces and 22 sites in China.

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7 333 Residents from 22 sites in Shanghai, Zhejiang, Jiangsu, Anhui and Jiangxi provinces were

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9 334 enrolled in SPECT-China study.
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335 **Table 1** Baseline characteristics between different groups.

Variables	Men (n=3682)	Women (n=5543)	P value
Age y	55.57±13.23	54.30±12.82	<0.001
FPG mmol/L	5.72±1.63	5.50±1.36	<0.001
HbA1c %	5.78±1.08	5.64±0.92	<0.001
TG mmol/L	1.88±1.79	1.55±1.20	<0.001
TC mmol/L	5.14±1.13	5.27±1.15	<0.001
LDL mmol/L	3.23±0.77	3.30±0.83	<0.001
HDL mmol/L	1.30±0.31	1.45±0.32	<0.001
UA umol/L	352.1±79.3	269.3±64.7	<0.001
BMI kg/m ²	25.11±3.45	24.40±3.67	<0.001
WC cm	85.85±9.42	78.72±9.90	<0.001
SBP mmHg	134.3±20.7	131.1±22.2	<0.001
DBP mmHg	82.1±12.9	77.8±12.9	<0.001
Diabetes %	16.3%	12.7%	<0.001
Hypertension %	53.4%	44.1%	<0.001

336 Uric acid: UA; Fasting plasma glucose: FPG; Alanine aminotransferase: ALT; Triglycerides: TG;

337 Total cholesterol: TC; Body mass index: BMI; Waist circumference: WC; Systolic blood pressure:

338 SBP; Diastolic blood pressure: DBP

Table 2 Characteristics of Eastern Chinese population.

	Percentage % (95%CI)				Means \pm SD		
	Diabetes	Hypertension	Smoking	Drinking	WC	SBP	BMI
Overall	14.1 (13.4, 14.8)	47.8 (46.8, 48.9)	19.2 (18.3, 20.0)	55.8 (54.8, 56.9)	81.57 \pm 10.32	132.4 \pm 21.7	24.68 \pm 3.60
Location							
Rural	15.8 (14.4, 17.2)	58.7 (56.8, 60.6)	22.9 (21.3, 24.5)	56.6 (54.7, 58.5)	83.14 \pm 10.38	139.7 \pm 23.2	24.71 \pm 3.65
Urban	13.4 (12.6, 14.2)	43.3 (42.1, 44.5)	17.6 (16.7, 18.6)	55.5 (54.3, 56.7)	80.90 \pm 10.23	129.4 \pm 20.3	24.67 \pm 3.58
Age groups							
<40	1.6 (0.9, 2.3)	11.1 (9.4, 12.9)	12.9 (11.0, 14.8)	42.0 (39.2, 44.7)	75.22 \pm 10.55	116.8 \pm 15.0	23.38 \pm 3.61
40-60	11.3 (10.3, 12.2)	41.8 (40.3, 43.3)	20.8 (19.6, 22.0)	54.9 (53.4, 56.5)	80.78 \pm 9.87	129.5 \pm 20.1	24.82 \pm 3.35
\geq 60	21.5 (20.2, 22.9)	67.1 (65.6, 68.7)	19.4 (18.1, 20.7)	61.5 (59.9, 63.1)	84.60 \pm 9.59	141.0 \pm 21.5	24.96 \pm 3.79
Economic status							
low	12.3 (11.3, 13.3)	47.8 (46.3, 49.4)	21.2 (19.9, 22.5)	46.6 (45.1, 48.2)	81.07 \pm 10.57	134.2 \pm 23.5	24.50 \pm 3.55
high	15.6 (14.6, 16.6)	47.8 (46.4, 49.2)	17.6 (16.5, 18.6)	62.9 (61.6, 64.3)	81.96 \pm 10.10	131.0 \pm 20.1	24.83 \pm 3.64
BMI							
<24	9.8 (8.9, 10.7)	35.2 (33.7, 36.7)	16.6 (15.4, 17.7)	52.9 (51.3, 54.5)	74.72 \pm 7.85	126.9 \pm 21.1	21.67 \pm 1.69
24-28	15.2 (14.0, 16.4)	53.0 (51.4, 54.7)	20.6 (19.2, 21.9)	58.3 (56.7, 59.9)	84.57 \pm 7.30	135.2 \pm 21.2	25.79 \pm 1.12
\geq 28	24.1 (21.8, 26.3)	69.1 (66.7, 71.5)	22.8 (20.6, 25.0)	57.6 (55.0, 60.2)	93.34 \pm 8.52	140.5 \pm 20.2	30.40 \pm 3.09
Glucose status							
normal	-	37.0 (35.6, 38.3)	16.2 (15.1, 17.2)	50.6 (49.3, 52.0)	78.95 \pm 9.88	128.0 \pm 20.6	24.08 \pm 3.44
prediabetes	-	57.6 (55.7, 59.5)	23.4 (21.7, 25.0)	63.2 (61.3, 65.1)	83.90 \pm 9.53	136.7 \pm 21.6	25.26 \pm 3.55
diabetes	-	72.7 (70.3, 75.2)	23.0 (20.6, 25.3)	61.3 (58.7, 64.0)	87.60 \pm 9.97	141.9 \pm 21.2	26.00 \pm 3.78

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Body mass index: BMI; Waist circumference: WC; Systolic blood pressure: SBP

Table 3 Biochemical index of Eastern Chinese population.

	Means \pm SD							
	UA	LDL	TG	HDL	TC	FPG	HbA1c	Creatinine
Overall	302.0 \pm 81.5	3.28 \pm 0.81	1.68 \pm 1.48	1.39 \pm 0.32	5.22 \pm 1.14	5.58 \pm 1.48	5.70 \pm 0.99	77.31 \pm 14.96
Location								
Rural	294.8 \pm 83.0	3.38 \pm 0.83	1.69 \pm 1.56	1.44 \pm 0.31	5.37 \pm 1.07	5.63 \pm 1.60	5.80 \pm 1.03	73.76 \pm 14.20
Urban	305.6 \pm 80.9	3.23 \pm 0.80	1.67 \pm 1.43	1.37 \pm 0.33	5.16 \pm 1.17	5.57 \pm 1.42	5.65 \pm 0.96	78.87 \pm 15.13
Age groups								
<40	294.1 \pm 85.7	2.81 \pm 0.65	1.35 \pm 1.25	1.39 \pm 0.30	4.60 \pm 0.87	4.98 \pm 0.76	5.09 \pm 0.57	75.82 \pm 14.73
40-60	298.0 \pm 82.8	3.29 \pm 0.78	1.76 \pm 1.71	1.39 \pm 0.32	5.24 \pm 1.16	5.52 \pm 1.46	5.62 \pm 0.94	76.26 \pm 14.59
\geq 60	310.1 \pm 78.3	3.42 \pm 0.83	1.69 \pm 1.20	1.38 \pm 0.34	5.39 \pm 1.13	5.86 \pm 1.60	5.98 \pm 1.04	79.09 \pm 15.47
Economic status								
low	299.8 \pm 85.1	3.23 \pm 0.82	1.70 \pm 1.65	1.45 \pm 0.32	5.20 \pm 1.05	5.54 \pm 1.48	5.62 \pm 0.99	76.29 \pm 15.23
high	304.4 \pm 78.7*	3.31 \pm 0.80*	1.66 \pm 1.31	1.34 \pm 0.32*	5.23 \pm 1.21	5.62 \pm 1.47*	5.75 \pm 0.98*	78.20 \pm 14.83*
BMI								
<24	279.5 \pm 73.3	3.15 \pm 0.80	1.35 \pm 1.05	1.48 \pm 0.33	5.11 \pm 1.09	5.39 \pm 1.35	5.53 \pm 0.92	75.83 \pm 14.26
24-28	313.9 \pm 81.7	3.36 \pm 0.81	1.85 \pm 1.50	1.33 \pm 0.30	5.28 \pm 1.18	5.64 \pm 1.47	5.76 \pm 0.99	78.34 \pm 15.37
\geq 28	335.5 \pm 85.3	3.44 \pm 0.80	2.20 \pm 2.13	1.27 \pm 0.28	5.39 \pm 1.17	6.00 \pm 1.74	6.02 \pm 1.10	78.95 \pm 15.44
Glucose status								
normal	294.9 \pm 81.3	3.12 \pm 0.76	1.54 \pm 1.38	1.41 \pm 0.32	5.05 \pm 1.10	5.09 \pm 0.54	5.16 \pm 0.36	76.81 \pm 14.77
prediabetes	313.1 \pm 81.1	3.51 \pm 0.81	1.71 \pm 1.17	1.38 \pm 0.32	5.49 \pm 1.12	5.45 \pm 0.72	5.93 \pm 0.20	77.95 \pm 14.83
diabetes	310.9 \pm 81.2	3.42 \pm 0.86	2.18 \pm 2.14	1.29 \pm 0.32	5.38 \pm 1.21	7.89 \pm 2.63	7.38 \pm 1.49	78.22 \pm 16.38

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3 Uric acid: UA; Triglycerides: TG; Total cholesterol: TC; Low-density lipoprotein: LDL;
4 High-density lipoprotein: HDL; Glycated hemoglobin: HbA1c; Fasting plasma glucose: FPG
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Table 4 Estimated prevalence of HUA in Eastern Chinese population.

	Percentage % (95%CI)		
	Overall	Men	Women
Overall	12.3 (11.6, 12.9)	17.9 (16.7-19.1)	8.5 (7.8-9.3)
Overall*	11.3 (9.9, 12.7)	20.7 (17.7, 23.7)	5.6 (4.3, 6.7)
Location			
Urban	12.9 (12.1, 13.7)	19.1 (17.6-20.7)	8.9 (8.0-9.8)
Rural	10.8 (9.6, 12.0)	15.2 (13.1-17.3)	7.7 (6.4-9.0)
Age groups			
<40	10.8 (9.0, 12.5)	22.8 (19.0, 26.6)	3.3 (2.0, 4.5)
40-60	11.2 (10.3, 12.2)	18.9 (17.0, 20.8)	6.5 (5.5, 7.4)
>=60	13.9 (12.8, 15.0)	15.4 (13.6, 17.2)	12.8 (11.4, 14.2)
Economic status			
low	11.8 (10.9-12.8)	18.3 (16.5-20.1)	7.2 (6.1-8.2)
high	12.6 (11.7-13.5)	17.5 (15.8-19.2)	9.5 (8.5-10.6)
BMI			
<24	6.7 (5.9, 7.5)	10.5 (8.9, 12.2)	4.8 (3.9, 5.6)
24-28	14.1 (13.0, 15.3)	19.9 (18.0, 21.9)	9.4 (8.1, 10.7)
>=28	22.5 (20.3, 24.6)	27.3 (23.9, 30.8)	18.5 (15.7, 21.2)
Glucose status			
normal	10.1 (9.3-10.9)	17.5 (15.8-19.2)	5.7 (4.9-6.5)
prediabetes	15.2 (13.9-16.6)	20.3 (17.9-22.7)	11.6 (10.0-13.2)
diabetes	15.1 (13.1-17.0)	15.0 (12.1-17.8)	15.2 (12.5-17.9)

Body mass index: BMI

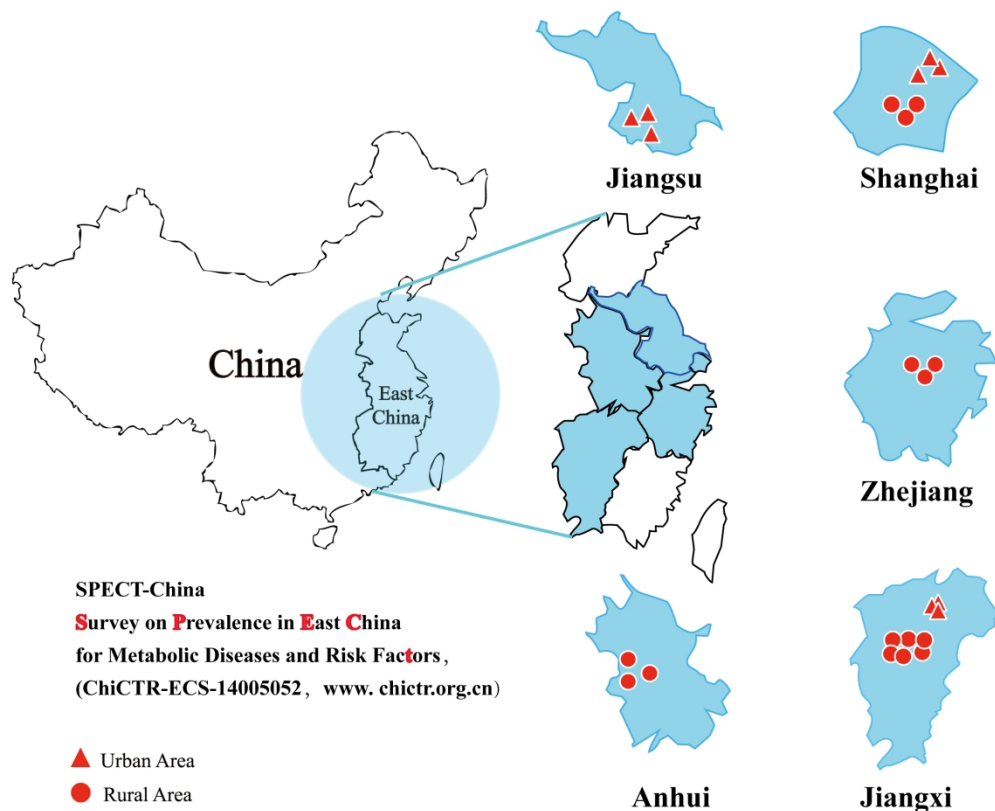
* standardized by proportions of population of 6th national population census data

Table 5 Risk factors for HUA in Eastern Chinese population.

Risk factors	OR	(95%CI)
Female sex	0.510	0.427, 0.609
Age per 10 years	1.041	0.976, 1.112
Urban residency	2.218	1.681, 2.927
≥Junior middle school education	1.042	0.866, 1.253
Lipids		
LDL per 1SD	1.018	0.888, 1.168
HDL per 1SD	0.936	0.850, 1.032
TC per 1SD	1.226	1.050, 1.432
TG per 1SD	1.672	1.491, 1.875
Current smoking	0.942	0.778, 1.141
Current drinking	0.913	0.784, 1.062
BMI		
Overweight	1.772	1.481, 2.120
Obesity	2.874	2.338, 3.532
Blood pressure		
SBP per 10mmHg	1.055	1.009, 1.103
DBP per 10mmHg	1.012	0.944, 1.085
High economic status	0.688	0.538, 0.879

Data are expressed as unStandardized B (95%CI). The enter procedure was used.

Body mass index: BMI



214x174mm (300 x 300 DPI)

Supplemental Table 1 Estimated prevalence of HUA (UA>420 μ mol/L) in Eastern Chinese population.

	Percentage % (95%CI)		
	Overall	Men	Women
Overall	8.4 (7.8, 9.0)	17.9 (16.7, 19.1)	2.1 (1.7, 2.5)
Overall*	8.8 (7.5, 10.1)	20.7 (17.7, 23.7)	1.4 (0.7, 2.0)
Location			
Urban	8.8 (8.1, 9.5)	19.1 (17.6-20.7)	2.1 (1.7, 2.6)
Rural	7.5 (6.5, 8.5)	15.2 (13.1-17.3)	1.9 (1.3, 2.6)
Age groups			
<40	9.3 (7.7, 10.9)	22.8 (19.0, 26.6)	0.9 (0.2, 1.6)
40-60	8.0 (7.2, 8.8)	18.9 (17.0, 20.8)	1.3 (0.8, 1.7)
>=60	8.5 (7.6, 9.4)	15.4 (13.6, 17.2)	3.5 (2.7, 4.2)
Economic status			
low	8.6 (7.7, 9.5)	18.3 (16.5-20.1)	1.6 (1.1, 2.0)
high	8.2 (7.5, 9.0)	17.5 (15.8-19.2)	2.5 (1.9, 3.0)
BMI			
<24	4.2 (3.6, 4.8)	10.5 (8.9, 12.2)	0.9 (0.6, 1.3)
24-28	10.1 (9.1, 11.1)	19.9 (18.0, 21.9)	2.1 (1.4, 2.7)
>=28	15.7 (13.8, 17.6)	27.3 (23.9, 30.8)	6.0 (4.4, 7.7)
Glucose status			
normal	7.3 (6.6, 8.0)	17.5 (15.8, 19.2)	1.1 (0.8, 1.5)
prediabetes	10.3 (9.1, 11.4)	20.3 (17.9, 22.7)	3.1 (2.2, 3.9)
diabetes	9.4 (7.8, 10.9)	15.0 (12.1, 17.8)	4.6 (3.0, 6.1)

Body mass index: BMI

* standardized by proportions of population of 6th national population census data

Supplemental table 2 Risk factors for HUA (UA>420 μ mol/L) in Eastern Chinese population.

Risk factors	OR	(95%CI)
Female sex	0.110	0.086, 0.142
Age per 10 years	0.937	0.867, 1.013
Urban residency	2.292	1.654, 3.176
\geq Junior middle school education	1.037	0.835, 1.288
Lipids		
LDL per 1SD	1.014	0.861, 1.193
HDL per 1SD	0.984	0.873, 1.109
TC per 1SD	1.209	1.004, 1.456
TG per 1SD	1.724	1.504, 1.978
Current smoking	0.921	0.755, 1.123
Current drinking	1.008	0.841, 1.209
BMI		
Overweight	1.812	1.448, 2.268
Obesity	2.835	2.191, 3.668
Blood pressure		
SBP per 10mmHg	1.082	1.023, 1.145
DBP per 10mmHg	1.017	0.932, 1.109
High economic status	0.670	0.504, 0.890

Data are expressed as unStandardized B (95%CI). The enter procedure was used.

Body mass index: BMI

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1,4
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1,4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
		(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	
Participants	6	<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	8
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	Not
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	Applicable
		Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8,9
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8,9
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
		(a) Describe all statistical methods, including those used to control for confounding	9
		(b) Describe any methods used to examine subgroups and interactions	9
		(c) Explain how missing data were addressed	8
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	
Statistical methods	12	<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	9
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	9

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	8
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not Applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Not Applicable
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Not Applicable
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(b) Report category boundaries when continuous variables were categorized	10
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not Applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10,11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other Information			

1	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2
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3 **Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

4 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is

5 best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and

6 Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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For peer review only

BMJ Open

Prevalence of hyperuricemia in an eastern Chinese population: a cross-sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-035614.R2
Article Type:	Original research
Date Submitted by the Author:	03-Mar-2020
Complete List of Authors:	Han, Bing; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Wang, Ningjian; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Chen, Yi; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Li, Qin; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Zhu, Chunfang ; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Chen, Yingchao; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Lu, Yingli; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology
Keywords:	General endocrinology < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY, Diabetes & endocrinology < INTERNAL MEDICINE

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3 **1 Prevalence of hyperuricemia in an eastern Chinese population: a cross-sectional**
4 **2 study**
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20 9 Running title: Prevalence of hyperuricemia in China.
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4 10 **ABSTRACT**

5 11 **Objectives:** In the past decade, China has been characterized by large-scale urbanization as
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7 12 well as rapid economic growth. The aim of this study was to further investigate the
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9 13 prevalence of hyperuricemia (HUA) in an eastern Chinese population.

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11 14 **Design:** Cross-sectional study.

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13 15 **Setting:** Survey of Prevalence in East China of Metabolic Diseases and Risk Factors
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15 16 (SPECT-China) study.

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17 17 **Participants:** In this study, 12,770 residents from 22 sites in eastern China were recruited.
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19 18 Finally, 9,225 subjects were included.

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21 19 **Main outcome measures:** The serum levels of uric acid, fasting plasma glucose (FPG),
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23 20 glycated hemoglobin (HbA1c) and other metabolic parameters were tested. Waist
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25 21 circumference (WC), weight, height and blood pressure were also measured. Questionnaires
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27 22 regarding smoking, drinking, education, etc., were collected from the subjects. HUA was
28
29 23 defined as serum UA >420 $\mu\text{mol/L}$ for men and >360 $\mu\text{mol/L}$ for women.

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31 24 **Results:** The prevalence of HUA in this eastern Chinese population was 11.3% (9.9, 12.7)
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33 25 overall, 20.7% (17.7, 23.7) in men and 5.6% (4.3, 6.7) in women. The prevalence of HUA in
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35 26 urban subjects was higher than that in rural subjects (12.9 vs. 10.8%, $P<0.01$). The prevalence
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37 27 of HUA was negatively and positively associated with age in men and women, respectively.
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39 28 Residents with high body mass index (BMI) levels had a higher prevalence of HUA. In the
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41 29 logistic regression analysis, male sex, urban residency, total cholesterol (TC), triglyceride
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43 30 (TG), overweight, obesity, systolic blood pressure (SBP) and low economic status were
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45 31 independently correlated with HUA.

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47 32 **Conclusions:** The estimated prevalence of HUA in this eastern Chinese population was
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49 33 11.3% (9.9, 12.7) overall and 20.7% (17.7, 23.7) and 5.6% (4.3, 6.7) in men and women,
50
51 34 respectively. HUA has gradually become an important public health issue in China.

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53 35 **Trial registration:** ChiCTR-ECS-14005052.

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55 36 **Keywords:** Prevalence, hyperuricemia, economic growth, public health, risk factors
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4 37 **Strengths and limitations of this study**

5 38 This is the largest published hyperuricemia study in an eastern Chinese population.

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7 39 This study covers residents from 22 sites in five provinces.

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9 40 This is a regional survey instead of a national study.

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11 41 We do not consider the influence of diet.
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4 42 **Abbreviations:** HUA, hyperuricemia; FPG, fasting plasma glucose; WC; waist
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6 43 circumference; BMI, body mass index; LDL, low-density lipoprotein; TG, triglyceride; HDL,
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8 44 high-density lipoprotein; TC, total cholesterol; HbA1c, Glycated hemoglobin; SBP, systolic
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10 45 blood pressure; DBP, diastolic blood pressure; NAFLD, Nonalcoholic fatty liver disease;
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12 46 CKD, chronic kidney disease; NGT, Normal glucose tolerance; GDP, gross domestic product;
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14 47 HPLC, high-performance liquid chromatography
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48 Introduction

49 In humans, uric acid (UA) is the end product of purine metabolism and is mainly excreted via
50 the kidneys. Xanthine oxidoreductase catalyzes two enzymatic reactions, hypoxanthine to
51 xanthine and xanthine to UA. Several conditions can influence the concentration of serum UA,
52 including purine-rich food intake, neoplastic disease, cytotoxic drugs, obesity, hypertension,
53 etc. [1-3].

54 Uric acid is reported to be associated with oxidative stress and inflammation [1, 4]. In
55 patients with hyperuricemia (HUA), deposition of UA in joints and tissues promotes the
56 occurrence of gout and chronic nephropathy. HUA has also been reported to be associated
57 with insulin resistance, nonalcoholic fatty liver disease (NAFLD) [5, 6], metabolic syndrome,
58 type 2 diabetes, atherosclerosis and coronary heart disease [7-11]. The overall prevalence of
59 HUA in adults in the United States was 21.4% in 2007-2008 [12]. In Henan Rural Cohort
60 Study conducted from 2015 to 2017, the crude and age-standardized prevalence of HUA were
61 10.24% and 12.60%, respectively[13]. In 2017, Chen Y et al found that the prevalence of
62 HUA was 13.4% in Jidong community of Tangshan City in northern China[14]. In an elderly
63 Chinese population of 7 areas, the overall prevalence of HUA was 13.1% in 2018 [15]. Liu R
64 et al [16] also conducted a meta-analysis including 38 regional studies between 2000 and
65 2014 to determine the prevalence of HUA in mainland China. The pooled prevalence of HUA
66 was 13.3% (male 19.4% and female 7.9%). These studies were all local or regional
67 investigations. There were also two national cross-sectional surveys using multistage,
68 stratified sampling. In 2009-2010, Liu H et al showed the adjusted prevalence of HUA was
69 8.4% in Chinese adults [17]. Recently, Lu X et al conducted a nationwide survey in 31
70 provinces in China. The prevalence of HUA were 13.7%-18.8% based on different urine
71 iodine concentrations[18].

72 In the past decade, China has been characterized by large-scale urbanization. The
73 percentage of the urban population rose from 18% in 1978 to 56% in 2015 [19]. As serum UA
74 is closely related to economic development and urbanization [13], it is necessary to
75 understand the latest prevalence of HUA in China.

76 China is characterized by regional and economic diversity. Eastern China has a relatively
77 higher economic status than the rest of the country. In the present study, we performed a

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78 cross-sectional survey to investigate the prevalence of HUA and its risk factors in an eastern
79 Chinese population.

80 **Methods**

81 **Study population**

82 Data from the current study are from the Survey of Prevalence in East China of Metabolic
83 Diseases and Risk Factors (SPECT-China), which is a population-based cross-sectional
84 survey of the prevalence of metabolic diseases and risk factors in eastern China [20]. The
85 registration number is ChiCTR-ECS-14005052 (www.chictr.org). In this study, 12,770
86 residents from 22 sites in Shanghai, Zhejiang, Jiangsu, Anhui and Jiangxi provinces were
87 enrolled from January 2014 to December 2015 (Supplemental Figure 1). The inclusion and
88 exclusion criteria were described previously [20]. Chinese citizens more than 18 years old
89 who had lived in their current area for more than 6 months were selected. We excluded
90 subjects with severe communication problems, acute illness, or an unwillingness to participate.
91 We also excluded residents who had no UA data (n=3,535) and chronic kidney disease (CKD)
92 stage 5 (n=10). Finally, 9,225 subjects were included. This study was approved by the ethics
93 committee of the Shanghai Ninth People's Hospital affiliated with Shanghai Jiaotong
94 University School of Medicine. Written consent was obtained from all the participants.

96 **Measurements and definition**

97 HUA was defined as serum UA >420 $\mu\text{mol/L}$ for men and >360 $\mu\text{mol/L}$ for women [21].
98 Blood pressure and heart rate were measured with a sphygmomanometer
99 (TERUMO-Elemano) three times. The mean of the three records was used in the analysis.
100 Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood
101 pressure (DBP) ≥ 90 mmHg or any self-reported history of hypertension. Diabetes was
102 defined as a self-reported history of diabetes or glycated hemoglobin (HbA1c) levels of 6.5%
103 or more. Prediabetes was defined as HbA1c concentrations between 5.7% and 6.4%. Normal
104 glucose tolerance (NGT) was defined as an HbA1c less than 5.7% [22]. Weight and height
105 were measured wearing light clothing and without shoes. Body mass index (BMI) was
106 calculated as weight (kg)/height squared (m^2). Overweight was defined as $24 \text{ kg/m}^2 \leq \text{BMI} < 28$
107 kg/m^2 . Obesity was defined as $\text{BMI} \geq 28 \text{ kg/m}^2$. Waist circumference (WC) was measured at
108 the level of 1 cm above the umbilicus. Demographic information and lifestyle risk factors
109 were gathered from standard questionnaires by trained staff. Current smoking was defined as

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4 110 having smoked at least 100 cigarettes in one's lifetime and currently smoking cigarettes [23].
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6 111 Current drinking was defined as drinking more than once a month. Current economic status
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8 112 was assessed by the gross domestic product (GDP) per capita of 2013 at each study site. The
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10 113 mean national GDP per capita (6807 US dollars from World Bank) in 2013 was considered
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12 114 the cutoff point for economic status.

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15 116 **Assessment of biochemical indexes**

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17 117 Venous blood samples were drawn from all participants after fasting for at least 8 hours and
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19 118 immediately centrifuged (2000 rpm for 15 min) at room temperature. Blood samples were
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21 119 stored at -20°C when collected and shipped by air in dry ice to one central laboratory certified
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23 120 by the College of American Pathologists within 2-4 hours of collection. All plasma and serum
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25 121 samples were frozen at -80°C after laboratory testing. Serum UA was analyzed with a
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27 122 Beckman Coulter AU 680 device with the original kit (Brea, California, USA). The validity
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29 123 and accuracy of UA were 6% and 4%, respectively. Other biochemical indexes were analyzed
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31 124 as described previously [24].

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34 126 **Statistical analysis**

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36 127 Statistical analysis was performed using IBM SPSS Statistics, Version 22 (IBM Corporation,
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38 128 Armonk, New York). Demographic and metabolic characteristics are expressed as the mean ±
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40 129 SD for continuous variables and percentages (95% CI) for categorical variables in the overall
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42 130 population and in subgroups of location, age, economic status, BMI and glucose status.
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44 131 Logistic analysis was used to investigate the association of demographic, lifestyle, and
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46 132 metabolic factors with the odds of HUA. According to the 6th national population census data,
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48 133 the proportions of the population in different age groups (<40, 40-60, ≥60) are 57.39%,
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50 134 29.29%, and 13.31% (total); 58.10%, 29.13%, and 12.76% (male); and 56.61%, 29.46%, and
51
52 135 13.91% (female), respectively [25]. Thus, we adjusted the prevalence of HUA by these
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54 136 proportions. All analyses were two-sided. $P < 0.05$ was considered significant.

137 **Results**

138 **Characteristics of this eastern Chinese population**

139 In our study, we analyzed UA in 9,225 Chinese adults, including 3,682 males (age,
140 55.57±13.23 y) and 5,543 females (age 54.30±12.82 y). The mean levels of serum UA were
141 352.12±79.30 nmol/L and 269.29±64.68 nmol/L in males and females, respectively. There
142 were significant sex differences in blood glucose, blood lipids, UA, BMI, WC and blood
143 pressure. The prevalence of diabetes and hypertension also showed a significant difference
144 (Table 1).

146 **Metabolic risk factors of this eastern Chinese population**

147 The prevalence of diabetes and hypertension, WC, SBP and BMI increased with age. As BMI
148 and glucose levels rose, the prevalence of hypertension, WC, SBP, BMI, triglyceride (TG),
149 FPG, and HbA1c increased. Moreover, people living in rural areas had a higher prevalence of
150 diabetes, WC, SBP, low-density lipoprotein (LDL), high-density lipoprotein (HDL), total
151 cholesterol (TC) and HbA1c. People with a high economic status had a higher prevalence of
152 diabetes, WC, UA, BMI, LDL, FPG, HbA1c and Cr (Tables 2, 3).

154 **Estimated prevalence of HUA in this eastern Chinese population**

155 The prevalence of HUA was 12.3% (11.6, 12.9), with 17.9% (16.7, 19.1) and 8.5% (7.8, 9.3)
156 in males and females, respectively. The prevalence of HUA in urban areas was higher than
157 that in rural areas (12.9% vs. 10.8%). The prevalence of HUA in developed areas was slightly
158 higher than that in underdeveloped areas (12.6% vs. 11.8%). As BMI increased, the
159 prevalence of HUA increased in both men and women. The prevalence of HUA in normal,
160 prediabetic and diabetic women were 5.7% (4.9, 6.5), 11.6% (10.0, 13.2) and 15.2% (12.5,
161 17.9) respectively (Table 4). So there was an increased trend of prevalence of HUA in women
162 with different glucose status. However, this trend was not obvious in men. After adjusting for
163 the proportions of the population in different age groups, the prevalence of HUA was 11.3%
164 (9.9, 12.7), with 20.7% (17.7, 23.7) and 5.6% (4.3, 6.7) in males and females, respectively
165 (Table 4).

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4 167 **Logistic regression analysis of HUA**

5 168 Male sex, urban residency, increased TC or TG, overweight, obesity, elevated SBP and low
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7 169 economic status were all risk factors for HUA in this eastern Chinese population (Table 5).
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9 170 However, increased age, higher educational status, increased LDL or HDL, current smoking
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11 171 or drinking and elevated DBP were not associated with the risk of HUA.
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172 Discussion

173 In this eastern Chinese population, the prevalence of HUA was 11.3%, which was similar to
174 the pooled prevalence reported in a systematic review performed in China (13.3%) [15].
175 However, this prevalence was more than that in the national HUA survey, which reported that
176 the prevalence of HUA was 8.4% [13]. The previous survey was performed in 2009-2010.
177 Our study occurred in 2014-2015. These two studies investigated different populations. In
178 addition, our prevalence was relatively lower than that in Qingdao, which is close to the sea
179 and where residents consume high amounts of seafood and beer [26]. Moreover, the
180 prevalence of HUA in our population was lower than those in the United States and Japan [12,
181 27], which might be attributed to economic status.

182 The prevalence of HUA in young men (<40 years) was seven times greater than that in
183 young women. However, as age increased, the prevalence of HUA gradually decreased in
184 men and increased in women, which was coincident with values previously reported [28]. In
185 residents more than 60 years of age, men and women had a similar prevalence of HUA. We
186 deduced that the diet of young men contains more purine than that of old men. The young
187 men also had an active metabolism. The prevalence of HUA was dramatically increased in
188 women older than 60 years, which might be caused by reduced estrogen levels.

189 Risk factors for HUA were also evaluated in our study. We found that male sex, urban
190 residency, hypertriglyceridemia, hypercholesterolemia, overweight, obesity, high SBP and
191 low economic status were risk factors for HUA. In previous studies, hypertriglyceridemia was
192 thought to be the strongest risk factor for HUA [28, 29]. However, the OR for HUA was 1.7
193 times with 1 SD elevation of triglyceridemia. In addition, obesity was the strongest risk factor
194 (OR=2.874) in our study. China has the largest obese population in the world [30]. In this
195 case, the prevalence of HUA will increase with the rising trend of obesity. Therefore, we
196 should pay more attention to prevent its consequences.

197 HUA is closely related to lifestyle and dietary habits. In previous studies, the prevalence of
198 HUA in urban areas was much greater than that in rural areas [13, 28]. In our study, the
199 prevalence of HUA in urban areas was mildly elevated (12.9% vs. 10.8%), and urbanization
200 was a risk factor for HUA. Eastern China is considered the developed area in the whole
201 country. Therefore, the difference between urban and rural areas was not obvious as in other

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202 places. Moreover, people with high economic status consumed more healthy food that
203 contained low purine ingredients. This could partly explain why low economic status became
204 a risk factor for HUA. In accordance with a previous study, smoking was not associated with
205 HUA [13]. However, according to a previous study, alcohol intake influences serum UA,
206 which is different from the results of our study. This difference might have been caused by
207 our definition of current drinking (current drinking was defined as drinking in the past 1
208 month), which mixed nonhabitual drinkers and habitual drinkers together.

209 As age increased, UA together with components of metabolic syndrome (FPG, SBP, WC)
210 also increased, which indicated that there might be a close relationship between metabolic
211 syndrome and HUA. Other studies have also found that HUA is associated with metabolic
212 syndrome [31, 32]. An epidemiologic study showed that HUA is positively correlated with
213 fasting serum insulin [33]. Krishnan et al reported that people with HUA have 1.36 times the
214 risk of developing insulin resistance in a 15-year follow-up study [34]. Thus, research has
215 indicated that insulin resistance plays an important role in the relationship between metabolic
216 syndrome and HUA [35].

217 There were several limitations in our study. First, this was not a national study but a local
218 survey. Second, we did not consider the influence of diet. Blood was drawn after fasting for
219 eight hours. However, the diet ingested near the blood drawing time was unknown. In
220 addition, this was a cross-sectional study. Therefore, we could not identify a causal
221 relationship between HUA and its risk factors.

222 In this study, we estimated the prevalence of HUA in an eastern Chinese population. To
223 prevent the prevalence of HUA, more attention should be paid to life status (such as economic
224 status and residence) and metabolic indexes (TC, TG, BMI, and SBP).

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4 225 **Acknowledgments**

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7 227 **Contributors**

9 228 YL and BH designed and supervised this investigation. BH performed this investigation. YC,
11 229 CFZ and YCC contributed to the data collection. NJW and QL provided technical or material
13 230 support. All authors read and approved the final manuscript.

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33 240 analysis, or interpretation of data or in the preparation, review, or approval of the article.

35 241 **Competing interests**

37 242 The authors have declared that no competing interests exist.

39 243 **Patient consent for publication**

41 244 Not required

43 245 **Ethical approval**

45 246 The study protocol was approved by the Institutional Review Board of the Shanghai Ninth
47 247 People's Hospital affiliated with Shanghai Jiaotong University School of Medicine.

49 248 **Provenance and peer review**

51 249 Not commissioned; externally peer reviewed.

53 250 **Data availability statement**

55 251 Data are available upon request to corresponding author.

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4 336 **Figure legend**

5 337 **Supplemental Figure 1** Position of the 5 provinces and 22 sites in China.

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7 338 Residents from 22 sites in Shanghai, Zhejiang, Jiangsu, Anhui and Jiangxi provinces were

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9 339 enrolled in SPECT-China study.
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340 **Table 1** Baseline characteristics between different groups.

Variables	Men (n=3682)	Women (n=5543)	P value
Age y	55.57±13.23	54.30±12.82	<0.001
FPG mmol/L	5.72±1.63	5.50±1.36	<0.001
HbA1c %	5.78±1.08	5.64±0.92	<0.001
TG mmol/L	1.88±1.79	1.55±1.20	<0.001
TC mmol/L	5.14±1.13	5.27±1.15	<0.001
LDL mmol/L	3.23±0.77	3.30±0.83	<0.001
HDL mmol/L	1.30±0.31	1.45±0.32	<0.001
UA umol/L	352.1±79.3	269.3±64.7	<0.001
BMI kg/m ²	25.11±3.45	24.40±3.67	<0.001
WC cm	85.85±9.42	78.72±9.90	<0.001
SBP mmHg	134.3±20.7	131.1±22.2	<0.001
DBP mmHg	82.1±12.9	77.8±12.9	<0.001
Diabetes %	16.3%	12.7%	<0.001
Hypertension %	53.4%	44.1%	<0.001

341 Uric acid: UA; Fasting plasma glucose: FPG; Alanine aminotransferase: ALT; Triglycerides: TG;

342 Total cholesterol: TC; Body mass index: BMI; Waist circumference: WC; Systolic blood pressure:

343 SBP; Diastolic blood pressure: DBP

Table 2 Characteristics of Eastern Chinese population.

	Percentage % (95%CI)				Means \pm SD		
	Diabetes	Hypertension	Smoking	Drinking	WC	SBP	BMI
Overall	14.1 (13.4, 14.8)	47.8 (46.8, 48.9)	19.2 (18.3, 20.0)	55.8 (54.8, 56.9)	81.57 \pm 10.32	132.4 \pm 21.7	24.68 \pm 3.60
Location							
Rural	15.8 (14.4, 17.2)	58.7 (56.8, 60.6)	22.9 (21.3, 24.5)	56.6 (54.7, 58.5)	83.14 \pm 10.38	139.7 \pm 23.2	24.71 \pm 3.65
Urban	13.4 (12.6, 14.2)	43.3 (42.1, 44.5)	17.6 (16.7, 18.6)	55.5 (54.3, 56.7)	80.90 \pm 10.23	129.4 \pm 20.3	24.67 \pm 3.58
Age groups							
<40	1.6 (0.9, 2.3)	11.1 (9.4, 12.9)	12.9 (11.0, 14.8)	42.0 (39.2, 44.7)	75.22 \pm 10.55	116.8 \pm 15.0	23.38 \pm 3.61
40-60	11.3 (10.3, 12.2)	41.8 (40.3, 43.3)	20.8 (19.6, 22.0)	54.9 (53.4, 56.5)	80.78 \pm 9.87	129.5 \pm 20.1	24.82 \pm 3.35
\geq 60	21.5 (20.2, 22.9)	67.1 (65.6, 68.7)	19.4 (18.1, 20.7)	61.5 (59.9, 63.1)	84.60 \pm 9.59	141.0 \pm 21.5	24.96 \pm 3.79
Economic status							
low	12.3 (11.3, 13.3)	47.8 (46.3, 49.4)	21.2 (19.9, 22.5)	46.6 (45.1, 48.2)	81.07 \pm 10.57	134.2 \pm 23.5	24.50 \pm 3.55
high	15.6 (14.6, 16.6)	47.8 (46.4, 49.2)	17.6 (16.5, 18.6)	62.9 (61.6, 64.3)	81.96 \pm 10.10	131.0 \pm 20.1	24.83 \pm 3.64
BMI							
<24	9.8 (8.9, 10.7)	35.2 (33.7, 36.7)	16.6 (15.4, 17.7)	52.9 (51.3, 54.5)	74.72 \pm 7.85	126.9 \pm 21.1	21.67 \pm 1.69
24-28	15.2 (14.0, 16.4)	53.0 (51.4, 54.7)	20.6 (19.2, 21.9)	58.3 (56.7, 59.9)	84.57 \pm 7.30	135.2 \pm 21.2	25.79 \pm 1.12
\geq 28	24.1 (21.8, 26.3)	69.1 (66.7, 71.5)	22.8 (20.6, 25.0)	57.6 (55.0, 60.2)	93.34 \pm 8.52	140.5 \pm 20.2	30.40 \pm 3.09
Glucose status							
normal	-	37.0 (35.6, 38.3)	16.2 (15.1, 17.2)	50.6 (49.3, 52.0)	78.95 \pm 9.88	128.0 \pm 20.6	24.08 \pm 3.44
prediabetes	-	57.6 (55.7, 59.5)	23.4 (21.7, 25.0)	63.2 (61.3, 65.1)	83.90 \pm 9.53	136.7 \pm 21.6	25.26 \pm 3.55
diabetes	-	72.7 (70.3, 75.2)	23.0 (20.6, 25.3)	61.3 (58.7, 64.0)	87.60 \pm 9.97	141.9 \pm 21.2	26.00 \pm 3.78

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Body mass index: BMI; Waist circumference: WC; Systolic blood pressure: SBP

Table 3 Biochemical index of Eastern Chinese population.

	Means \pm SD							
	UA	LDL	TG	HDL	TC	FPG	HbA1c	Creatinine
Overall	302.0 \pm 81.5	3.28 \pm 0.81	1.68 \pm 1.48	1.39 \pm 0.32	5.22 \pm 1.14	5.58 \pm 1.48	5.70 \pm 0.99	77.31 \pm 14.96
Location								
Rural	294.8 \pm 83.0	3.38 \pm 0.83	1.69 \pm 1.56	1.44 \pm 0.31	5.37 \pm 1.07	5.63 \pm 1.60	5.80 \pm 1.03	73.76 \pm 14.20
Urban	305.6 \pm 80.9	3.23 \pm 0.80	1.67 \pm 1.43	1.37 \pm 0.33	5.16 \pm 1.17	5.57 \pm 1.42	5.65 \pm 0.96	78.87 \pm 15.13
Age groups								
<40	294.1 \pm 85.7	2.81 \pm 0.65	1.35 \pm 1.25	1.39 \pm 0.30	4.60 \pm 0.87	4.98 \pm 0.76	5.09 \pm 0.57	75.82 \pm 14.73
40-60	298.0 \pm 82.8	3.29 \pm 0.78	1.76 \pm 1.71	1.39 \pm 0.32	5.24 \pm 1.16	5.52 \pm 1.46	5.62 \pm 0.94	76.26 \pm 14.59
\geq 60	310.1 \pm 78.3	3.42 \pm 0.83	1.69 \pm 1.20	1.38 \pm 0.34	5.39 \pm 1.13	5.86 \pm 1.60	5.98 \pm 1.04	79.09 \pm 15.47
Economic status								
low	299.8 \pm 85.1	3.23 \pm 0.82	1.70 \pm 1.65	1.45 \pm 0.32	5.20 \pm 1.05	5.54 \pm 1.48	5.62 \pm 0.99	76.29 \pm 15.23
high	304.4 \pm 78.7*	3.31 \pm 0.80*	1.66 \pm 1.31	1.34 \pm 0.32*	5.23 \pm 1.21	5.62 \pm 1.47*	5.75 \pm 0.98*	78.20 \pm 14.83*
BMI								
<24	279.5 \pm 73.3	3.15 \pm 0.80	1.35 \pm 1.05	1.48 \pm 0.33	5.11 \pm 1.09	5.39 \pm 1.35	5.53 \pm 0.92	75.83 \pm 14.26
24-28	313.9 \pm 81.7	3.36 \pm 0.81	1.85 \pm 1.50	1.33 \pm 0.30	5.28 \pm 1.18	5.64 \pm 1.47	5.76 \pm 0.99	78.34 \pm 15.37
\geq 28	335.5 \pm 85.3	3.44 \pm 0.80	2.20 \pm 2.13	1.27 \pm 0.28	5.39 \pm 1.17	6.00 \pm 1.74	6.02 \pm 1.10	78.95 \pm 15.44
Glucose status								
normal	294.9 \pm 81.3	3.12 \pm 0.76	1.54 \pm 1.38	1.41 \pm 0.32	5.05 \pm 1.10	5.09 \pm 0.54	5.16 \pm 0.36	76.81 \pm 14.77
prediabetes	313.1 \pm 81.1	3.51 \pm 0.81	1.71 \pm 1.17	1.38 \pm 0.32	5.49 \pm 1.12	5.45 \pm 0.72	5.93 \pm 0.20	77.95 \pm 14.83
diabetes	310.9 \pm 81.2	3.42 \pm 0.86	2.18 \pm 2.14	1.29 \pm 0.32	5.38 \pm 1.21	7.89 \pm 2.63	7.38 \pm 1.49	78.22 \pm 16.38

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Uric acid: UA; Triglycerides: TG; Total cholesterol: TC; Low-density lipoprotein: LDL;
High-density lipoprotein: HDL; Glycated hemoglobin: HbA1c; Fasting plasma glucose: FPG

Table 4 Estimated prevalence of HUA in Eastern Chinese population.

	Percentage % (95%CI)		
	Overall	Men	Women
Overall	12.3 (11.6, 12.9)	17.9 (16.7-19.1)	8.5 (7.8-9.3)
Overall*	11.3 (9.9, 12.7)	20.7 (17.7, 23.7)	5.6 (4.3, 6.7)
Location			
Urban	12.9 (12.1, 13.7)	19.1 (17.6-20.7)	8.9 (8.0-9.8)
Rural	10.8 (9.6, 12.0)	15.2 (13.1-17.3)	7.7 (6.4-9.0)
Age groups			
<40	10.8 (9.0, 12.5)	22.8 (19.0, 26.6)	3.3 (2.0, 4.5)
40-60	11.2 (10.3, 12.2)	18.9 (17.0, 20.8)	6.5 (5.5, 7.4)
≥60	13.9 (12.8, 15.0)	15.4 (13.6, 17.2)	12.8 (11.4, 14.2)
Economic status			
low	11.8 (10.9-12.8)	18.3 (16.5-20.1)	7.2 (6.1-8.2)
high	12.6 (11.7-13.5)	17.5 (15.8-19.2)	9.5 (8.5-10.6)
BMI			
<24	6.7 (5.9, 7.5)	10.5 (8.9, 12.2)	4.8 (3.9, 5.6)
24-28	14.1 (13.0, 15.3)	19.9 (18.0, 21.9)	9.4 (8.1, 10.7)
≥28	22.5 (20.3, 24.6)	27.3 (23.9, 30.8)	18.5 (15.7, 21.2)
Glucose status			
normal	10.1 (9.3-10.9)	17.5 (15.8-19.2)	5.7 (4.9-6.5)
prediabetes	15.2 (13.9-16.6)	20.3 (17.9-22.7)	11.6 (10.0-13.2)
diabetes	15.1 (13.1-17.0)	15.0 (12.1-17.8)	15.2 (12.5-17.9)

Body mass index: BMI

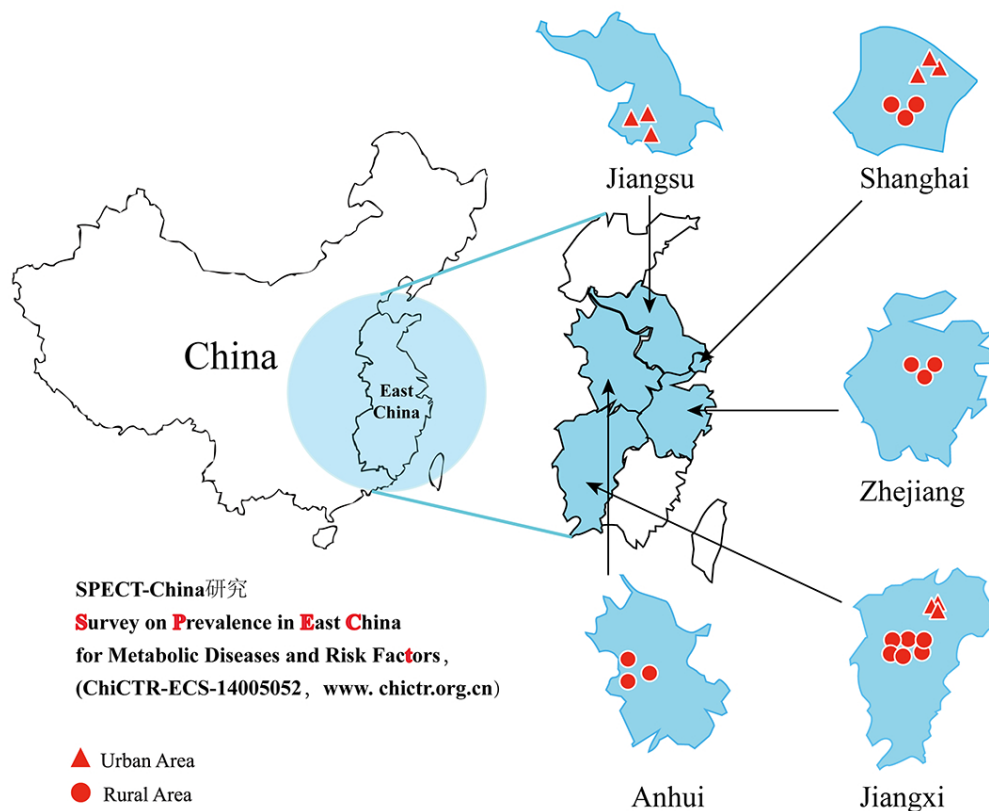
* standardized by proportions of population of 6th national population census data

Table 5 Risk factors for HUA in Eastern Chinese population.

Risk factors	OR	(95%CI)
Female sex	0.510	0.427, 0.609
Age per 10 years	1.041	0.976, 1.112
Urban residency	2.218	1.681, 2.927
≥Junior middle school education	1.042	0.866, 1.253
Lipids		
LDL per 1SD	1.018	0.888, 1.168
HDL per 1SD	0.936	0.850, 1.032
TC per 1SD	1.226	1.050, 1.432
TG per 1SD	1.672	1.491, 1.875
Current smoking	0.942	0.778, 1.141
Current drinking	0.913	0.784, 1.062
BMI		
Overweight	1.772	1.481, 2.120
Obesity	2.874	2.338, 3.532
Blood pressure		
SBP per 10mmHg	1.055	1.009, 1.103
DBP per 10mmHg	1.012	0.944, 1.085
High economic status	0.688	0.538, 0.879

Data are expressed as unStandardized B (95%CI). The enter procedure was used.

Body mass index: BMI



STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	Not
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	Applicable
		Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	8
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy			
		(e) Describe any sensitivity analyses	8

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	7
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not Applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Not Applicable
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Not Applicable
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9
		(b) Report category boundaries when continuous variables were categorized	9
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not Applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9,10
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other Information			

1	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13
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3 **Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

4 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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For peer review only

BMJ Open

Prevalence of hyperuricemia in an eastern Chinese population: a cross-sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-035614.R3
Article Type:	Original research
Date Submitted by the Author:	19-Mar-2020
Complete List of Authors:	Han, Bing; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Wang, Ningjian; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Chen, Yi; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Li, Qin; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Zhu, Chunfang ; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Chen, Yingchao; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine Lu, Yingli; Shanghai 9th Peoples Hospital Affiliated to Shanghai Jiaotong University School of Medicine
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology
Keywords:	General endocrinology < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY, Diabetes & endocrinology < INTERNAL MEDICINE

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3 **1 Prevalence of hyperuricemia in an eastern Chinese population: a cross-sectional**
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7 3 Bing Han*, Ningjian Wang, Yi Chen, Qin Li, Chunfang Zhu, Yingchao Chen and Yingli Lu*
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20 9 Running title: Prevalence of hyperuricemia in China.
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4 10 **ABSTRACT**

5 11 **Objectives:** In the past decade, China has been characterized by large-scale urbanization as
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7 12 well as rapid economic growth. The aim of this study was to further investigate the
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9 13 prevalence of hyperuricemia (HUA) in an eastern Chinese population.

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11 14 **Design:** Cross-sectional study.

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13 15 **Setting:** Survey of Prevalence in East China of Metabolic Diseases and Risk Factors
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15 16 (SPECT-China) study.

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17 17 **Participants:** In this study, 12,770 residents from 22 sites in eastern China were recruited.
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19 18 Finally, 9,225 subjects were included.

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21 19 **Main outcome measures:** The serum levels of uric acid, fasting plasma glucose (FPG),
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23 20 glycated hemoglobin (HbA1c) and other metabolic parameters were tested. Waist
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25 21 circumference (WC), weight, height and blood pressure were also measured. Questionnaires
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27 22 regarding smoking, drinking, education, etc., were collected from the subjects. HUA was
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29 23 defined as serum UA >420 $\mu\text{mol/L}$ for men and >360 $\mu\text{mol/L}$ for women.

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31 24 **Results:** The prevalence of HUA in this eastern Chinese population was 11.3% (9.9, 12.7)
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33 25 overall, 20.7% (17.7, 23.7) in men and 5.6% (4.3, 6.7) in women. The prevalence of HUA in
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35 26 urban subjects was higher than that in rural subjects (12.9 vs. 10.8%, $P<0.01$). The prevalence
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37 27 of HUA was negatively and positively associated with age in men and women, respectively.
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39 28 Residents with high body mass index (BMI) levels had a higher prevalence of HUA. In the
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41 29 logistic regression analysis, male sex, urban residency, total cholesterol (TC), triglyceride
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43 30 (TG), overweight, obesity, systolic blood pressure (SBP) and low economic status were
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45 31 independently correlated with HUA.

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47 32 **Conclusions:** The estimated prevalence of HUA in this eastern Chinese population was
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49 33 11.3% (9.9, 12.7) overall and 20.7% (17.7, 23.7) and 5.6% (4.3, 6.7) in men and women,
50
51 34 respectively. HUA has gradually become an important public health issue in China.

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53 35 **Trial registration:** ChiCTR-ECS-14005052.

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55 36 **Keywords:** Prevalence, hyperuricemia, economic growth, public health, risk factors
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4 37 **Strengths and limitations of this study**

5 38 This is the largest published hyperuricemia study in an eastern Chinese population.

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7 39 This study covers residents from 22 sites in five provinces.

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9 40 This is a regional survey instead of a national study.

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11 41 We do not consider the influence of diet.
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4 42 **Abbreviations:** HUA, hyperuricemia; FPG, fasting plasma glucose; WC; waist
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6 43 circumference; BMI, body mass index; LDL, low-density lipoprotein; TG, triglyceride; HDL,
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8 44 high-density lipoprotein; TC, total cholesterol; HbA1c, Glycated hemoglobin; SBP, systolic
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10 45 blood pressure; DBP, diastolic blood pressure; NAFLD, Nonalcoholic fatty liver disease;
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12 46 CKD, chronic kidney disease; NGT, Normal glucose tolerance; GDP, gross domestic product;
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14 47 HPLC, high-performance liquid chromatography
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48 **Introduction**

49 In humans, uric acid (UA) is the end product of purine metabolism and is mainly excreted via
50 the kidneys. Xanthine oxidoreductase catalyzes two enzymatic reactions, hypoxanthine to
51 xanthine and xanthine to UA. Several conditions can influence the concentration of serum UA,
52 including purine-rich food intake, neoplastic disease, cytotoxic drugs, obesity, hypertension,
53 etc. [1-3].

54 Uric acid is reported to be associated with oxidative stress and inflammation [1, 4]. In
55 patients with hyperuricemia (HUA), deposition of UA in joints and tissues promotes the
56 occurrence of gout and chronic nephropathy. HUA has also been reported to be associated
57 with insulin resistance, nonalcoholic fatty liver disease (NAFLD) [5, 6], metabolic syndrome,
58 type 2 diabetes, atherosclerosis and coronary heart disease [7-11]. The overall prevalence of
59 HUA in adults in the United States was 21.4% in 2007-2008 [12]. In 2009-2010, Liu H et al
60 showed the adjusted prevalence of HUA was 8.4% in Chinese adults [13]. Recently, Lu X et
61 al conducted a nationwide survey in 31 provinces in China. The prevalence of HUA were
62 13.7%-18.8% based on different urine iodine concentrations[14]. These studies were national
63 cross-sectional surveys using multistage, stratified sampling. There were also several local or
64 regional investigations. In Henan Rural Cohort Study conducted from 2015 to 2017, the crude
65 and age-standardized prevalence of HUA were 10.24% and 12.60%, respectively[15]. In 2017,
66 Chen Y et al found that the prevalence of HUA was 13.4% in Jidong community of Tangshan
67 City in northern China[16]. In an elderly Chinese population of 7 areas, the overall prevalence
68 of HUA was 13.1% in 2018 [17]. Liu R et al [18] also conducted a meta-analysis including 38
69 regional studies between 2000 and 2014 to determine the prevalence of HUA in mainland
70 China. The pooled prevalence of HUA was 13.3% (male 19.4% and female 7.9%).

71 In the past decade, China has been characterized by large-scale urbanization. The
72 percentage of the urban population rose from 18% in 1978 to 56% in 2015 [19]. As serum UA
73 is closely related to economic development and urbanization [15], it is necessary to
74 understand the latest prevalence of HUA in China.

75 China is characterized by regional and economic diversity. Eastern China has a relatively
76 higher economic status than the rest of the country. In the present study, we performed a
77 cross-sectional survey to investigate the prevalence of HUA and its risk factors in an eastern

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78 Chinese population.

79 **Methods**

80 **Study population**

81 Data from the current study are from the Survey of Prevalence in East China of Metabolic
82 Diseases and Risk Factors (SPECT-China), which is a population-based cross-sectional
83 survey of the prevalence of metabolic diseases and risk factors in eastern China [20]. The
84 registration number is ChiCTR-ECS-14005052 (www.chictr.org). 12,770 residents from 22
85 sites in five provinces (Shanghai, Zhejiang, Jiangsu, Anhui and Jiangxi) were recruited from
86 January 2014 to December 2015 (Supplemental Figure 1). The inclusion and exclusion
87 criteria were described previously [20]. Local residents more than 18 years old and lived in
88 their current area for more than 6 months were included in this study. We excluded subjects
89 with severe communication problems, acute illness, or an unwillingness to participate. We
90 also excluded residents who had no UA data (n=3,535) and chronic kidney disease (CKD)
91 stage 5 (n=10). Finally, 9,225 subjects were included. This study was approved by the ethics
92 committee of the Shanghai Ninth People's Hospital affiliated with Shanghai Jiaotong
93 University School of Medicine. Informed consent was obtained from all the participants.

95 **Measurements and definition**

96 HUA was defined as serum UA >420 $\mu\text{mol/L}$ for men and >360 $\mu\text{mol/L}$ for women [21].
97 Blood pressure and heart rate were measured with a sphygmomanometer
98 (TERUMO-Elemano) three times. Mean value of the three records was used in the analysis.
99 Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood
100 pressure (DBP) ≥ 90 mmHg or any self-reported history of hypertension. Diabetes was
101 defined as a self-reported history of diabetes or glycated hemoglobin (HbA1c) levels of 6.5%
102 or more. Prediabetes was defined as HbA1c concentrations between 5.7% and 6.4%. Normal
103 glucose tolerance (NGT) was defined as an HbA1c less than 5.7% [22]. Weight, height and
104 waist circumference (WC) were measured by standard procedure. Body mass index (BMI)
105 was calculated as weight (kg) divided by height squared (m^2). Overweight and obesity were
106 defined as $24 \text{ kg/m}^2 \leq \text{BMI} < 28 \text{ kg/m}^2$ and $\text{BMI} \geq 28 \text{ kg/m}^2$, respectively. Demographic
107 characteristics and lifestyle risk factors were collected by standard questionnaires. Current
108 smoking, drinking and economic status were defined as previously described [23,24].

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4 1095 110 **Assessment of biochemical indexes**

7 111 After fasting for 8 hours, venous blood samples were drawn from all participants and quickly
8 112 centrifuged at room temperature. Within 2-4 hours of collection, blood samples were stored at
9 113 -20°C and transported by air in dry ice to one central laboratory certified by the College of
10 114 American Pathologists as previously described [25]. Serum UA was analyzed with a
11 115 Beckman Coulter AU 680 device with the original kit (Brea, California, USA). The validity
12 116 and accuracy of UA were 6% and 4%, respectively. Other biochemical indexes were analyzed
13 117 as described previously [26].
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24 119 **Statistical analysis**

25 120 We performed statistical analysis by IBM SPSS Version 22 (IBM Corporation, Armonk, New
26 121 York). Demographic and metabolic characteristics are expressed as the mean \pm SD for
27 122 continuous variables and percentages (95% CI) for categorical variables in the overall
28 123 population and in subgroups of location, age, economic status, BMI and glucose status.
29 124 Logistic analysis was used to investigate the association of demographic, lifestyle, and
30 125 metabolic factors with the odds of HUA. According to the 6th national population census data,
31 126 the proportions of the population in different age groups (<40, 40-60, \geq 60) are 57.39%,
32 127 29.29%, and 13.31% (total); 58.10%, 29.13%, and 12.76% (male); and 56.61%, 29.46%, and
33 128 13.91% (female), respectively [27]. Thus, we adjusted the prevalence of HUA by these
34 129 proportions. All analyses were two-sided. $P < 0.05$ was considered significant.
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47 131 **Patient and public involvement**

48 132 Patients and the public were not involved in the development of research questions, design of
49 133 the study, recruitment and conduct of the study or dissemination of the study results.
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134 **Results**

135 **Characteristics of this eastern Chinese population**

136 In our study, we analyzed UA in 9,225 Chinese adults, including 3,682 males (age,
137 55.57±13.23 y) and 5,543 females (age 54.30±12.82 y). The mean levels of serum UA were
138 352.12±79.30 nmol/L and 269.29±64.68 nmol/L in males and females, respectively. There
139 were significant sex differences in blood glucose, blood lipids, UA, BMI, WC and blood
140 pressure. The prevalence of diabetes and hypertension also showed a significant difference
141 (Table 1).

143 **Metabolic risk factors of this eastern Chinese population**

144 The prevalence of diabetes and hypertension, WC, SBP and BMI increased with age. As BMI
145 and glucose levels rose, the prevalence of hypertension, WC, SBP, BMI, triglyceride (TG),
146 FPG, and HbA1c increased. Moreover, people living in rural areas had a higher prevalence of
147 diabetes, WC, SBP, low-density lipoprotein (LDL), high-density lipoprotein (HDL), total
148 cholesterol (TC) and HbA1c. People with a high economic status had a higher prevalence of
149 diabetes, WC, UA, BMI, LDL, FPG, HbA1c and Cr (Tables 2, 3).

151 **Estimated prevalence of HUA in this eastern Chinese population**

152 The prevalence of HUA was 12.3% (11.6, 12.9), with 17.9% (16.7, 19.1) and 8.5% (7.8, 9.3)
153 in males and females, respectively. The prevalence of HUA in urban areas was higher than
154 that in rural areas (12.9% vs. 10.8%). The prevalence of HUA in developed areas was slightly
155 higher than that in underdeveloped areas (12.6% vs. 11.8%). As BMI increased, the
156 prevalence of HUA increased in both men and women. The prevalence of HUA in normal,
157 prediabetic and diabetic women were 5.7% (4.9, 6.5), 11.6% (10.0, 13.2) and 15.2% (12.5,
158 17.9) respectively (Table 4). So there was an increased trend of prevalence of HUA in women
159 with different glucose status. However, this trend was not obvious in men. After adjusting for
160 the proportions of the population in different age groups, the prevalence of HUA was 11.3%
161 (9.9, 12.7), with 20.7% (17.7, 23.7) and 5.6% (4.3, 6.7) in males and females, respectively
162 (Table 4). When HUA was defined as serum UA of more than 420 µmol/L in both men and
163 women, the prevalence of HUA was 8.4% (7.8, 9.0) in total and 2.1% (1.7, 2.5) in females.

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4 164 After adjusting for the proportions of the population in different age groups, the prevalence of
5 165 HUA was 8.8% (7.5, 10.1) in total and 1.4% (0.7, 2.0) in females (Supplemental Table 1).

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9 167 **Logistic regression analysis of HUA**

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11 168 Male sex, urban residency, increased TC or TG, overweight, obesity, elevated SBP and low
12 169 economic status were all risk factors for HUA in this eastern Chinese population (Table 5).

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14 170 However, increased age, higher educational status, increased LDL or HDL, current smoking
15 171 or drinking and elevated DBP were not associated with the risk of HUA. When HUA was
16 172 defined as serum UA of more than 420 $\mu\text{mol/L}$ in both men and women, the association was
17 173 similar to the above results (Supplemental Table 2).

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174 Discussion

175 In this eastern Chinese population, the prevalence of HUA was 11.3%, which was similar to
176 the pooled prevalence reported in a systematic review performed in China (13.3%) [18].
177 However, this prevalence was more than that in the national HUA survey, which reported that
178 the prevalence of HUA was 8.4% in 2009-2010 [13]. These two studies investigated different
179 populations. Recently, a national study was performed on the relationship between
180 hyperuricemia and iodine intake. The prevalence of hyperuricemia was 17.8%, 18.8%, 16.0%
181 and 13.7% in the urinary iodine concentrations (UICs) <100, 100-199, 200-299, and
182 ≥ 300 ug/L groups [14]. Our result was between these national surveys, which was performed
183 in 2014-2015. As a regional study, the prevalence of our result was similar to other regional
184 investigations in China[15-18]. However, our prevalence was relatively lower than that in
185 Qingdao, Shandong Province, which is close to the sea and where residents consume high
186 amounts of seafood and beer [28]. Moreover, the prevalence of HUA in our population was
187 lower than those in the United States and Japan [12, 29], which might be attributed to
188 economic status.

189 The prevalence of HUA in young men (<40 years) was seven times greater than that in
190 young women. However, as age increased, the prevalence of HUA gradually decreased in
191 men and increased in women, which was coincident with values previously reported [30]. In
192 residents more than 60 years of age, men and women had a similar prevalence of HUA. We
193 deduced that the diet of young men contains more purine than that of old men. The young
194 men also had an active metabolism. The prevalence of HUA was dramatically increased in
195 women older than 60 years, which might be caused by reduced estrogen levels.

196 Risk factors for HUA were also evaluated in our study. We found that male sex, urban
197 residency, hypertriglyceridemia, hypercholesterolemia, overweight, obesity, high SBP and
198 low economic status were risk factors for HUA. In previous studies, hypertriglyceridemia was
199 thought to be the strongest risk factor for HUA [30, 31]. However, the OR for HUA was 1.7
200 times with 1 SD elevation of triglyceridemia. In addition, obesity was the strongest risk factor
201 (OR=2.874) in our study. China has the largest obese population in the world [32]. In this
202 case, the prevalence of HUA will increase with the rising trend of obesity. Therefore, we
203 should pay more attention to prevent its consequences.

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4 204 HUA is closely related to lifestyle and dietary habits. In previous studies, the prevalence of
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6 205 HUA in urban areas was much greater than that in rural areas [13, 30]. In our study, the
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8 206 prevalence of HUA in urban areas was mildly elevated (12.9% vs. 10.8%), and urbanization
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10 207 was a risk factor for HUA. Eastern China is considered the developed area in the whole
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12 208 country. Therefore, the difference between urban and rural areas was not obvious as in other
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14 209 places. Moreover, people with high economic status consumed more healthy food that
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16 210 contained low purine ingredients. This could partly explain why low economic status became
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18 211 a risk factor for HUA. In accordance with a previous study, smoking was not associated with
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20 212 HUA [13]. However, according to a previous study, alcohol intake influences serum UA,
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22 213 which is different from the results of our study. This difference might have been caused by
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24 214 our definition of current drinking (current drinking was defined as drinking in the past 1
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26 215 month), which mixed nonhabitual drinkers and habitual drinkers together.

27 216 As age increased, UA together with components of metabolic syndrome (FPG, SBP, WC)
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29 217 also increased, which indicated that there might be a close relationship between metabolic
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31 218 syndrome and HUA. Other studies have also found that HUA is associated with metabolic
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33 219 syndrome [33, 34]. An epidemiologic study showed that HUA is positively correlated with
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35 220 fasting serum insulin [35]. Krishnan et al reported that people with HUA have 1.36 times the
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37 221 risk of developing insulin resistance in a 15-year follow-up study [36]. Thus, research has
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39 222 indicated that insulin resistance plays an important role in the relationship between metabolic
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41 223 syndrome and HUA [37].

42 224 There were several limitations in our study. First, this was not a national study but a local
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44 225 survey. Second, we did not consider the influence of diet. Blood was drawn after fasting for
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46 226 eight hours. However, the diet ingested near the blood drawing time was unknown. In
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48 227 addition, this was a cross-sectional study. Therefore, we could not identify a causal
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50 228 relationship between HUA and its risk factors.

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52 229 In this study, we estimated the prevalence of HUA in an eastern Chinese population. To
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54 230 prevent the prevalence of HUA, more attention should be paid to life status (such as economic
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56 231 status and residence) and metabolic indexes (TC, TG, BMI, and SBP).
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4 232 **Acknowledgments**

5 233 We thank all the participants in the study.

7 234 **Contributors**

9 235 YL and BH designed and supervised this investigation. BH performed this investigation. YC,
11 236 CFZ and YCC contributed to the data collection. NJW and QL provided technical or material
13 237 support. All authors read and approved the final manuscript.

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33 247 analysis, or interpretation of data or in the preparation, review, or approval of the article.

35 248 **Competing interests**

37 249 The authors have declared that no competing interests exist.

39 250 **Patient consent for publication**

41 251 Not required

43 252 **Ethical approval**

45 253 The study protocol was approved by the Institutional Review Board of the Shanghai Ninth
47 254 People's Hospital affiliated with Shanghai Jiaotong University School of Medicine.

49 255 **Provenance and peer review**

51 256 Not commissioned; externally peer reviewed.

53 257 **Data availability statement**

55 258 Data are available upon request to corresponding author.
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4 348 **Figure legend**

5 349 **Supplemental Figure 1** Position of the 5 provinces and 22 sites in China.

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7 350 Residents from 22 sites in Shanghai, Zhejiang, Jiangsu, Anhui and Jiangxi provinces were

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9 351 enrolled in SPECT-China study.
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352 **Table 1** Baseline characteristics between different groups.

Variables	Men (n=3682)	Women (n=5543)	P value
Age y	55.57±13.23	54.30±12.82	<0.001
FPG mmol/L	5.72±1.63	5.50±1.36	<0.001
HbA1c %	5.78±1.08	5.64±0.92	<0.001
TG mmol/L	1.88±1.79	1.55±1.20	<0.001
TC mmol/L	5.14±1.13	5.27±1.15	<0.001
LDL mmol/L	3.23±0.77	3.30±0.83	<0.001
HDL mmol/L	1.30±0.31	1.45±0.32	<0.001
UA umol/L	352.1±79.3	269.3±64.7	<0.001
BMI kg/m ²	25.11±3.45	24.40±3.67	<0.001
WC cm	85.85±9.42	78.72±9.90	<0.001
SBP mmHg	134.3±20.7	131.1±22.2	<0.001
DBP mmHg	82.1±12.9	77.8±12.9	<0.001
Diabetes %	16.3%	12.7%	<0.001
Hypertension %	53.4%	44.1%	<0.001

353 Uric acid: UA; Fasting plasma glucose: FPG; Alanine aminotransferase: ALT; Triglycerides: TG;

354 Total cholesterol: TC; Body mass index: BMI; Waist circumference: WC; Systolic blood pressure:

355 SBP; Diastolic blood pressure: DBP

Table 2 Characteristics of Eastern Chinese population.

	Percentage % (95%CI)				Means \pm SD		
	Diabetes	Hypertension	Smoking	Drinking	WC	SBP	BMI
Overall	14.1 (13.4, 14.8)	47.8 (46.8, 48.9)	19.2 (18.3, 20.0)	55.8 (54.8, 56.9)	81.57 \pm 10.32	132.4 \pm 21.7	24.68 \pm 3.60
Location							
Rural	15.8 (14.4, 17.2)	58.7 (56.8, 60.6)	22.9 (21.3, 24.5)	56.6 (54.7, 58.5)	83.14 \pm 10.38	139.7 \pm 23.2	24.71 \pm 3.65
Urban	13.4 (12.6, 14.2)	43.3 (42.1, 44.5)	17.6 (16.7, 18.6)	55.5 (54.3, 56.7)	80.90 \pm 10.23	129.4 \pm 20.3	24.67 \pm 3.58
Age groups							
<40	1.6 (0.9, 2.3)	11.1 (9.4, 12.9)	12.9 (11.0, 14.8)	42.0 (39.2, 44.7)	75.22 \pm 10.55	116.8 \pm 15.0	23.38 \pm 3.61
40-60	11.3 (10.3, 12.2)	41.8 (40.3, 43.3)	20.8 (19.6, 22.0)	54.9 (53.4, 56.5)	80.78 \pm 9.87	129.5 \pm 20.1	24.82 \pm 3.35
\geq 60	21.5 (20.2, 22.9)	67.1 (65.6, 68.7)	19.4 (18.1, 20.7)	61.5 (59.9, 63.1)	84.60 \pm 9.59	141.0 \pm 21.5	24.96 \pm 3.79
Economic status							
low	12.3 (11.3, 13.3)	47.8 (46.3, 49.4)	21.2 (19.9, 22.5)	46.6 (45.1, 48.2)	81.07 \pm 10.57	134.2 \pm 23.5	24.50 \pm 3.55
high	15.6 (14.6, 16.6)	47.8 (46.4, 49.2)	17.6 (16.5, 18.6)	62.9 (61.6, 64.3)	81.96 \pm 10.10	131.0 \pm 20.1	24.83 \pm 3.64
BMI							
<24	9.8 (8.9, 10.7)	35.2 (33.7, 36.7)	16.6 (15.4, 17.7)	52.9 (51.3, 54.5)	74.72 \pm 7.85	126.9 \pm 21.1	21.67 \pm 1.69
24-28	15.2 (14.0, 16.4)	53.0 (51.4, 54.7)	20.6 (19.2, 21.9)	58.3 (56.7, 59.9)	84.57 \pm 7.30	135.2 \pm 21.2	25.79 \pm 1.12
\geq 28	24.1 (21.8, 26.3)	69.1 (66.7, 71.5)	22.8 (20.6, 25.0)	57.6 (55.0, 60.2)	93.34 \pm 8.52	140.5 \pm 20.2	30.40 \pm 3.09
Glucose status							
normal	-	37.0 (35.6, 38.3)	16.2 (15.1, 17.2)	50.6 (49.3, 52.0)	78.95 \pm 9.88	128.0 \pm 20.6	24.08 \pm 3.44
prediabetes	-	57.6 (55.7, 59.5)	23.4 (21.7, 25.0)	63.2 (61.3, 65.1)	83.90 \pm 9.53	136.7 \pm 21.6	25.26 \pm 3.55
diabetes	-	72.7 (70.3, 75.2)	23.0 (20.6, 25.3)	61.3 (58.7, 64.0)	87.60 \pm 9.97	141.9 \pm 21.2	26.00 \pm 3.78

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Body mass index: BMI; Waist circumference: WC; Systolic blood pressure: SBP

Table 3 Biochemical index of Eastern Chinese population.

	Means \pm SD							
	UA	LDL	TG	HDL	TC	FPG	HbA1c	Creatinine
Overall	302.0 \pm 81.5	3.28 \pm 0.81	1.68 \pm 1.48	1.39 \pm 0.32	5.22 \pm 1.14	5.58 \pm 1.48	5.70 \pm 0.99	77.31 \pm 14.96
Location								
Rural	294.8 \pm 83.0	3.38 \pm 0.83	1.69 \pm 1.56	1.44 \pm 0.31	5.37 \pm 1.07	5.63 \pm 1.60	5.80 \pm 1.03	73.76 \pm 14.20
Urban	305.6 \pm 80.9	3.23 \pm 0.80	1.67 \pm 1.43	1.37 \pm 0.33	5.16 \pm 1.17	5.57 \pm 1.42	5.65 \pm 0.96	78.87 \pm 15.13
Age groups								
<40	294.1 \pm 85.7	2.81 \pm 0.65	1.35 \pm 1.25	1.39 \pm 0.30	4.60 \pm 0.87	4.98 \pm 0.76	5.09 \pm 0.57	75.82 \pm 14.73
40-60	298.0 \pm 82.8	3.29 \pm 0.78	1.76 \pm 1.71	1.39 \pm 0.32	5.24 \pm 1.16	5.52 \pm 1.46	5.62 \pm 0.94	76.26 \pm 14.59
\geq 60	310.1 \pm 78.3	3.42 \pm 0.83	1.69 \pm 1.20	1.38 \pm 0.34	5.39 \pm 1.13	5.86 \pm 1.60	5.98 \pm 1.04	79.09 \pm 15.47
Economic status								
low	299.8 \pm 85.1	3.23 \pm 0.82	1.70 \pm 1.65	1.45 \pm 0.32	5.20 \pm 1.05	5.54 \pm 1.48	5.62 \pm 0.99	76.29 \pm 15.23
high	304.4 \pm 78.7*	3.31 \pm 0.80*	1.66 \pm 1.31	1.34 \pm 0.32*	5.23 \pm 1.21	5.62 \pm 1.47*	5.75 \pm 0.98*	78.20 \pm 14.83*
BMI								
<24	279.5 \pm 73.3	3.15 \pm 0.80	1.35 \pm 1.05	1.48 \pm 0.33	5.11 \pm 1.09	5.39 \pm 1.35	5.53 \pm 0.92	75.83 \pm 14.26
24-28	313.9 \pm 81.7	3.36 \pm 0.81	1.85 \pm 1.50	1.33 \pm 0.30	5.28 \pm 1.18	5.64 \pm 1.47	5.76 \pm 0.99	78.34 \pm 15.37
\geq 28	335.5 \pm 85.3	3.44 \pm 0.80	2.20 \pm 2.13	1.27 \pm 0.28	5.39 \pm 1.17	6.00 \pm 1.74	6.02 \pm 1.10	78.95 \pm 15.44
Glucose status								
normal	294.9 \pm 81.3	3.12 \pm 0.76	1.54 \pm 1.38	1.41 \pm 0.32	5.05 \pm 1.10	5.09 \pm 0.54	5.16 \pm 0.36	76.81 \pm 14.77
prediabetes	313.1 \pm 81.1	3.51 \pm 0.81	1.71 \pm 1.17	1.38 \pm 0.32	5.49 \pm 1.12	5.45 \pm 0.72	5.93 \pm 0.20	77.95 \pm 14.83
diabetes	310.9 \pm 81.2	3.42 \pm 0.86	2.18 \pm 2.14	1.29 \pm 0.32	5.38 \pm 1.21	7.89 \pm 2.63	7.38 \pm 1.49	78.22 \pm 16.38

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3 Uric acid: UA; Triglycerides: TG; Total cholesterol: TC; Low-density lipoprotein: LDL;
4 High-density lipoprotein: HDL; Glycated hemoglobin: HbA1c; Fasting plasma glucose: FPG
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Table 4 Estimated prevalence of HUA in Eastern Chinese population.

	Percentage % (95%CI)		
	Overall	Men	Women
Overall	12.3 (11.6, 12.9)	17.9 (16.7-19.1)	8.5 (7.8-9.3)
Overall*	11.3 (9.9, 12.7)	20.7 (17.7, 23.7)	5.6 (4.3, 6.7)
Location			
Urban	12.9 (12.1, 13.7)	19.1 (17.6-20.7)	8.9 (8.0-9.8)
Rural	10.8 (9.6, 12.0)	15.2 (13.1-17.3)	7.7 (6.4-9.0)
Age groups			
<40	10.8 (9.0, 12.5)	22.8 (19.0, 26.6)	3.3 (2.0, 4.5)
40-60	11.2 (10.3, 12.2)	18.9 (17.0, 20.8)	6.5 (5.5, 7.4)
>=60	13.9 (12.8, 15.0)	15.4 (13.6, 17.2)	12.8 (11.4, 14.2)
Economic status			
low	11.8 (10.9-12.8)	18.3 (16.5-20.1)	7.2 (6.1-8.2)
high	12.6 (11.7-13.5)	17.5 (15.8-19.2)	9.5 (8.5-10.6)
BMI			
<24	6.7 (5.9, 7.5)	10.5 (8.9, 12.2)	4.8 (3.9, 5.6)
24-28	14.1 (13.0, 15.3)	19.9 (18.0, 21.9)	9.4 (8.1, 10.7)
>=28	22.5 (20.3, 24.6)	27.3 (23.9, 30.8)	18.5 (15.7, 21.2)
Glucose status			
normal	10.1 (9.3-10.9)	17.5 (15.8-19.2)	5.7 (4.9-6.5)
prediabetes	15.2 (13.9-16.6)	20.3 (17.9-22.7)	11.6 (10.0-13.2)
diabetes	15.1 (13.1-17.0)	15.0 (12.1-17.8)	15.2 (12.5-17.9)

Body mass index: BMI

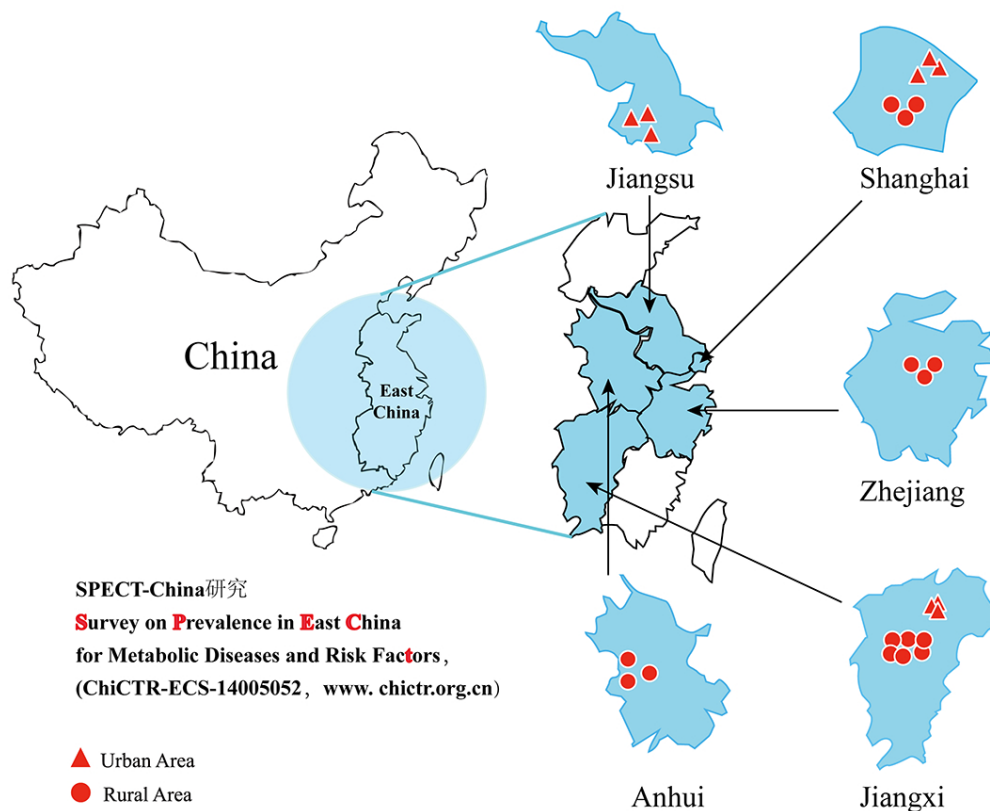
* standardized by proportions of population of 6th national population census data

Table 5 Risk factors for HUA in Eastern Chinese population.

Risk factors	OR	(95%CI)
Female sex	0.510	0.427, 0.609
Age per 10 years	1.041	0.976, 1.112
Urban residency	2.218	1.681, 2.927
≥Junior middle school education	1.042	0.866, 1.253
Lipids		
LDL per 1SD	1.018	0.888, 1.168
HDL per 1SD	0.936	0.850, 1.032
TC per 1SD	1.226	1.050, 1.432
TG per 1SD	1.672	1.491, 1.875
Current smoking	0.942	0.778, 1.141
Current drinking	0.913	0.784, 1.062
BMI		
Overweight	1.772	1.481, 2.120
Obesity	2.874	2.338, 3.532
Blood pressure		
SBP per 10mmHg	1.055	1.009, 1.103
DBP per 10mmHg	1.012	0.944, 1.085
High economic status	0.688	0.538, 0.879

Data are expressed as unStandardized B (95%CI). The enter procedure was used.

Body mass index: BMI



Supplemental Table 1 Estimated prevalence of HUA (UA>420 μ mol/L) in Eastern Chinese population.

	Percentage % (95%CI)	
	Overall	Women
Overall	8.4 (7.8, 9.0)	2.1 (1.7, 2.5)
Overall*	8.8 (7.5, 10.1)	1.4 (0.7, 2.0)
Location		
Urban	8.8 (8.1, 9.5)	2.1 (1.7, 2.6)
Rural	7.5 (6.5, 8.5)	1.9 (1.3, 2.6)
Age groups		
<40	9.3 (7.7, 10.9)	0.9 (0.2, 1.6)
40-60	8.0 (7.2, 8.8)	1.3 (0.8, 1.7)
\geq 60	8.5 (7.6, 9.4)	3.5 (2.7, 4.2)
Economic status		
low	8.6 (7.7, 9.5)	1.6 (1.1, 2.0)
high	8.2 (7.5, 9.0)	2.5 (1.9, 3.0)
BMI		
<24	4.2 (3.6, 4.8)	0.9 (0.6, 1.3)
24-28	10.1 (9.1, 11.1)	2.1 (1.4, 2.7)
\geq 28	15.7 (13.8, 17.6)	6.0 (4.4, 7.7)
Glucose status		
normal	7.3 (6.6, 8.0)	1.1 (0.8, 1.5)
prediabetes	10.3 (9.1, 11.4)	3.1 (2.2, 3.9)
diabetes	9.4 (7.8, 10.9)	4.6 (3.0, 6.1)

Body mass index: BMI

* standardized by proportions of population of 6th national population census data

Supplemental table 2 Risk factors for HUA (UA>420 μ mol/L) in Eastern Chinese population.

Risk factors	OR	(95%CI)
Female sex	0.110	0.086, 0.142
Age per 10 years	0.937	0.867, 1.013
Urban residency	2.292	1.654, 3.176
\geq Junior middle school education	1.037	0.835, 1.288
Lipids		
LDL per 1SD	1.014	0.861, 1.193
HDL per 1SD	0.984	0.873, 1.109
TC per 1SD	1.209	1.004, 1.456
TG per 1SD	1.724	1.504, 1.978
Current smoking	0.921	0.755, 1.123
Current drinking	1.008	0.841, 1.209
BMI		
Overweight	1.812	1.448, 2.268
Obesity	2.835	2.191, 3.668
Blood pressure		
SBP per 10mmHg	1.082	1.023, 1.145
DBP per 10mmHg	1.017	0.932, 1.109
High economic status	0.670	0.504, 0.890

Data are expressed as unStandardized B (95%CI). The enter procedure was used.

Body mass index: BMI

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	Not
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	Applicable
		Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7,8
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7,8
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	8
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	8

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	7
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	Not Applicable
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Not Applicable
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Not Applicable
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10
		(b) Report category boundaries when continuous variables were categorized	10
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not Applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10,11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other Information			

1	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14
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3 **Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

4 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is

5 best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and

6 Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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